

=> d his full

(FILE 'HOME' ENTERED AT 08:25:08 ON 24 JUN 2005)

FILE 'REGISTRY' ENTERED AT 08:25:33 ON 24 JUN 2005  
ACT AUD807F0/Q

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L1      STR
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L2      STR L1
        D QUE L2
L3      SCR 1841
L4      SCR 2039 OR 2041 OR 2050 OR 2049 OR 2053 OR 2052 OR 2048 OR 204
L5      0 SEA CSS SAM L2 AND L3 NOT L4

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FILE 'HCAPLUS' ENTERED AT 08:30:49 ON 24 JUN 2005

L6 1 SEA ABB=ON PLU=ON (GB99-17793# OR WO2000-GB2903#)/AP,RPN

FILE 'REGISTRY' ENTERED AT 08:32:01 ON 24 JUN 2005

FILE 'HCAPLUS' ENTERED AT 08:32:03 ON 24 JUN 2005

L7 TRA L6 1- RN : 65 TERMS

FILE 'REGISTRY' ENTERED AT 08:32:03 ON 24 JUN 2005

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L8      65 SEA ABB=ON PLU=ON L7
L9      16 SEA ABB=ON PLU=ON L8 AND NR>=4
L10     256861 SEA ABB=ON PLU=ON C5-C6-C6-C6/ES
L11     STR L2
L12     35 SEA SUB=L10 CSS SAM L11 AND L3 NOT L4
L13     0 SEA SUB=L10 CSS SAM L2 AND L3 NOT L4
L14     4008 SEA SUB=L10 CSS FUL L11 AND L3 NOT L4
        D QUE L2
L15     4 SEA SUB=L14 SSS SAM L2
        D SCA
L16     106 SEA SUB=L14 SSS FUL L2
        SAV TEM L14 AUD807F0/A
        SAV TEM L16 AUD807S0/A

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FILE 'HCAPLUS' ENTERED AT 08:44:01 ON 24 JUN 2005

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L17     246 SEA ABB=ON PLU=ON ("MORRISON J"/AU OR "MORRISON J D"/AU)
        E MORRISON JAMES/AU
L18     22 SEA ABB=ON PLU=ON ("MORRISON JAMES"/AU OR "MORRISON JAMES
        DUNCAN"/AU)
        E MORRISON JIM/AU
L19     4 SEA ABB=ON PLU=ON "MORRISON JIM"/AU
        E LUCAS M/AU
L20     190 SEA ABB=ON PLU=ON ("LUCAS M"/AU OR "LUCAS M L"/AU)
        E LUCAS MIKE/AU
        E LUCAS MICHAEL/AU
L21     17 SEA ABB=ON PLU=ON ("LUCAS MICHAEL"/AU OR "LUCAS MICHAEL
        L"/AU OR "LUCAS MICHAEL LESLIE"/AU)
        E WHEELER S/AU
L22     56 SEA ABB=ON PLU=ON ("WHEELER S"/AU OR "WHEELER S A"/AU OR
        "WHEELER S C"/AU OR "WHEELER S E"/AU OR "WHEELER S F"/AU OR
        "WHEELER S G"/AU OR "WHEELER S H"/AU OR "WHEELER S J"/AU OR
        "WHEELER S JAMES"/AU OR "WHEELER S L"/AU OR "WHEELER S M"/AU
        OR "WHEELER S R"/AU OR "WHEELER S S"/AU OR "WHEELER S T"/AU OR
        "WHEELER S V"/AU)
        E WHEELER SARAH/AU
L23     16 SEA ABB=ON PLU=ON ("WHEELER SARAH"/AU OR "WHEELER SARAH
        C"/AU OR "WHEELER SARAH CAROLINE"/AU OR "WHEELER SARAH E"/AU
        OR "WHEELER SARAH J"/AU OR "WHEELER SARAH L"/AU)
L24     90 SEA ABB=ON PLU=ON L16
L25     QUE ABB=ON PLU=ON DRUG DELIVERY SYSTEMS+OLD,NT/CT
L26     0 SEA ABB=ON PLU=ON L24 AND L25

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Search done by Noble Jarrell

L27 8 SEA ABB=ON PLU=ON L24 AND ?CONJUGAT?  
 L28 0 SEA ABB=ON PLU=ON L16/D  
 L29 0 SEA ABB=ON PLU=ON L24 AND (L17 OR L18 OR L19 OR L20 OR L21 OR L22)  
 L30 5 SEA ABB=ON PLU=ON L14 AND (L17 OR L18 OR L19 OR L20 OR L21 OR L22)  
 L31 17638 SEA ABB=ON PLU=ON L14 NOT L30  
 L32 2551 SEA ABB=ON PLU=ON L31 AND ?CONJUGAT?  
 L33 134 SEA ABB=ON PLU=ON L32 AND L25  
 L34 QUE ABB=ON PLU=ON PY<=1999 OR AY<=1999 OR PRY<=1999 OR PD<19990730 OR AD<19990730 OR PRD<19990730  
 L35 64 SEA ABB=ON PLU=ON L33 AND L34  
 L36 7 SEA ABB=ON PLU=ON L27 AND L34  
 L37 8 SEA ABB=ON PLU=ON L27 OR L36  
 SEL AN L35 4 5 11 16 18 20-21 25 29 31-33 43-44 48 50  
 L38 16 SEA ABB=ON PLU=ON ("119:146497"/AN OR "120:173477"/AN OR "121:286635"/AN OR "123:322102"/AN OR "126:308684"/AN OR "126:347323"/AN OR "127:99659"/AN OR "128:286354"/AN OR "130:213559"/AN OR "131:314185"/AN OR "132:26813"/AN OR "132:313463"/AN OR "132:73648"/AN OR "133:140227"/AN OR "136:107571"/AN OR "136:665"/AN OR "1993:546497"/AN OR "1994:173477"/AN OR "1994:686635"/AN OR "1995:721131"/AN OR "1997:218959"/AN OR "1997:372273"/AN OR "1997:463447"/AN OR "1998:208387"/AN OR "1999:185918"/AN OR "1999:708452"/AN OR "1999:722480"/AN OR "1999:764076"/AN OR "2000:10612"/AN OR "2000:508917"/AN OR "2001:844884"/AN OR "2002:72799"/AN) AND L35  
 SEL AN 1 2 5 8 16 L38  
 L39 11 SEA ABB=ON PLU=ON L38 NOT ("119:146497"/AN OR "130:213559"/AN OR "132:26813"/AN OR "136:107571"/AN OR "136:665"/AN OR "1993:546497"/AN OR "1999:185918"/AN OR "1999:764076"/AN OR "2001:844884"/AN OR "2002:72799"/AN)  
 L40 19 SEA ABB=ON PLU=ON L37 OR L39  
  
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 L41 0 SEA ABB=ON PLU=ON L16  
 L42 11483 SEA ABB=ON PLU=ON L14  
 L43 1146 SEA ABB=ON PLU=ON L42 AND ?CONJUGAT?  
 E ORAL/CT  
 E E5+ALL  
 E E2+ALL  
 L44 109 SEA ABB=ON PLU=ON ORAL DRUG ADMINISTRATION/CT AND L43  
 E MORRISON J/AU  
 L45 338 SEA ABB=ON PLU=ON ("MORRISON J"/AU OR "MORRISON J D"/AU)  
 E MORRISON JIM/AU  
 E MORRISON JAMES/AU  
 E LUCAS M/AU  
 L46 326 SEA ABB=ON PLU=ON ("LUCAS M"/AU OR "LUCAS M L"/AU)  
 E LUCAS MICHAEL/AU  
 E WHEELER S/AU  
 L47 151 SEA ABB=ON PLU=ON ("WHEELER S"/AU OR "WHEELER S A"/AU OR "WHEELER S B"/AU OR "WHEELER S C"/AU OR "WHEELER S D"/AU OR "WHEELER S E"/AU OR "WHEELER S F"/AU OR "WHEELER S G"/AU OR "WHEELER S H"/AU OR "WHEELER S J"/AU OR "WHEELER S K"/AU OR "WHEELER S L"/AU OR "WHEELER S M"/AU OR "WHEELER S R"/AU OR "WHEELER S V"/AU OR "WHEELER S W"/AU)  
 L48 4 SEA ABB=ON PLU=ON L42 AND (L45 OR L46 OR L47)  
 L49 109 SEA ABB=ON PLU=ON L44 NOT L48  
 L50 91 SEA ABB=ON PLU=ON L49 AND PY<=1999

FILE 'EMBASE' ENTERED AT 09:33:50 ON 24 JUN 2005

SEL AN L50 60 63 40 43 46 12 16 20 29 2 3 5  
 L51 12 SEA ABB=ON PLU=ON (1999046272/AN OR 1999256785/AN OR 1999324376/AN OR 84147710/AN OR 85080967/AN OR 88276787/AN OR 89150062/AN OR 90226900/AN OR 92292458/AN OR 94299511/AN OR 95240331/AN OR 96132330/AN) AND L50

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FILE 'BIOSIS' ENTERED AT 09:34:08 ON 24 JUN 2005
L52      9899 SEA ABB=ON  PLU=ON  L14 OR L16
L53      1104 SEA ABB=ON  PLU=ON  L52 AND ?CONJUGAT?
          E MORRISON J/AU
L54      392 SEA ABB=ON  PLU=ON  ("MORRISON J"/AU OR "MORRISON J D"/AU)
          E MORRISON JAMES/AU
L55      4 SEA ABB=ON  PLU=ON  ("MORRISON JAMES"/AU OR "MORRISON JAMES
          D"/AU)
          E M LUCAS M/AU
          E LUCAS M/AU
L56      280 SEA ABB=ON  PLU=ON  ("LUCAS M"/AU OR "LUCAS M L"/AU)
          E LUCAS MICHAEL/AU
L57      3 SEA ABB=ON  PLU=ON  ("LUCAS MICHAEL"/AU OR "LUCAS MICHAEL
          L"/AU)
          E WHEELER S/AU
L58      160 SEA ABB=ON  PLU=ON  ("WHEELER S"/AU OR "WHEELER S A"/AU OR
          "WHEELER S C"/AU OR "WHEELER S CHRISTIAN"/AU OR "WHEELER S
          D"/AU OR "WHEELER S E"/AU OR "WHEELER S F"/AU OR "WHEELER S
          G"/AU OR "WHEELER S G B"/AU OR "WHEELER S H"/AU OR "WHEELER S
          J"/AU OR "WHEELER S JAMES"/AU OR "WHEELER S K"/AU OR "WHEELER
          S L"/AU OR "WHEELER S M"/AU OR "WHEELER S P"/AU OR "WHEELER S
          R"/AU OR "WHEELER S V"/AU OR "WHEELER S W"/AU)
          E WHEELER SARA/AU
L59      21 SEA ABB=ON  PLU=ON  ("WHEELER SARAH"/AU OR "WHEELER SARAH
          C"/AU OR "WHEELER SARAH E"/AU OR "WHEELER SARAH L"/AU OR
          "WHEELER SCHILLING T"/AU)
L60      1 SEA ABB=ON  PLU=ON  L53 AND (L54 OR L55 OR L56 OR L57 OR L58
          OR L59)

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=> b reg

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STRUCTURE FILE UPDATES: 23 JUN 2005 HIGHEST RN 852898-09-0  
 DICTIONARY FILE UPDATES: 23 JUN 2005 HIGHEST RN 852898-09-0

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*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
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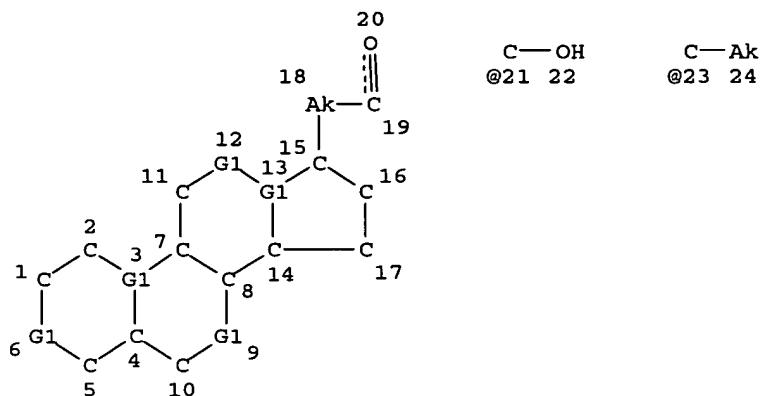
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
 information enter HELP PROP at an arrow prompt in the file or refer  
 to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d que sta l14

Search done by Noble Jarrell

L3 SCR 1841  
 L4 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2053 OR 2052 OR 2048 O  
 R 2043 OR 2054  
 L10 256861 SEA FILE=REGISTRY ABB=ON PLU=ON C5-C6-C6-C6/ES  
 L11 STR



VAR G1=C/21/23  
 NODE ATTRIBUTES:  
 CONNECT IS M1 RC AT 19  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

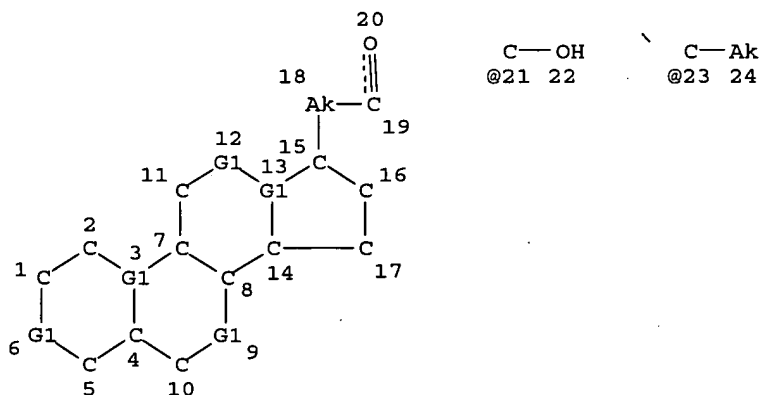
GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE  
 L14 4008 SEA FILE=REGISTRY SUB=L10 CSS FUL L11 AND L3 NOT L4

100.0% PROCESSED 201370 ITERATIONS  
 SEARCH TIME: 00.00.10

4008 ANSWERS

=> d que sta l16  
 L2 STR



VAR G1=C/21/23  
 NODE ATTRIBUTES:  
 CONNECT IS M1 RC AT 19  
 DEFAULT MLEVEL IS ATOM  
 GGCAT IS UNS AT 18  
 DEFAULT ECLEVEL IS LIMITED

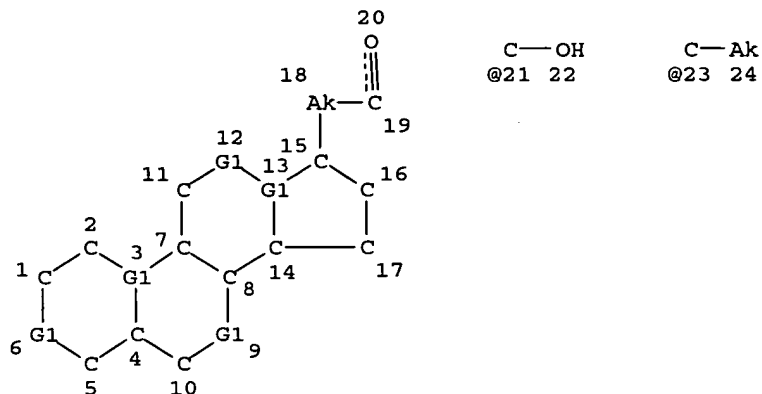
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## GRAPH ATTRIBUTES:

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NUMBER OF NODES IS 24

## STEREO ATTRIBUTES: NONE

L3 SCR 1841  
L4 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2053 OR 2052 OR 2048 O  
R 2043 OR 2054  
L10 256861 SEA FILE=REGISTRY ABB=ON PLU=ON C5-C6-C6-C6/ES  
L11 STR



VAR G1=C/21/23

## NODE ATTRIBUTES:

CONNECT IS M1 RC AT 19  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 24

## STEREO ATTRIBUTES: NONE

L14 4008 SEA FILE=REGISTRY SUB=L10 CSS FUL L11 AND L3 NOT L4  
L16 106 SEA FILE=REGISTRY SUB=L14 SSS FUL L2

100.0% PROCESSED 4008 ITERATIONS  
SEARCH TIME: 00.00.01

106 ANSWERS

=> b heap

FILE 'HCAPLUS' ENTERED AT 09:38:45 ON 24 JUN 2005  
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FILE COVERS 1907 - 24 Jun 2005 VOL 143 ISS 1  
FILE LAST UPDATED: 23 Jun 2005 (20050623/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all fhitstr 130 tot

L30 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2004:394158 HCAPLUS  
 DN 141:47626  
 ED Entered STN: 14 May 2004  
 TI Absorption of the cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo  
 AU McHarg, S.; Morton, J. S.; McGinn, B. J.; Yasin, M.; Morrison, J. D.  
 CS Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, UK  
 SO Acta Physiologica Scandinavica (2004), 181(1), 23-34  
 CODEN: APSCAX; ISSN: 0001-6772  
 PB Blackwell Publishing Ltd.  
 DT Journal  
 LA English  
 CC 2-6 (Mammalian Hormones)  
 AB Previously, the authors demonstrated that gastrin peptides as long as 34 amino acids were absorbed from the ileum of rat after conjugation to the C24 position of cholic acid and that these peptides retained full biol. activity. As absorption was specific to the ileum, it was inferred that the conjugated hormone was taken up by the bile salt transporters. The authors have now extended these expts. to a member of a different family of hormones, viz. secretin, a 27-amino acid hormone that stimulates serous secretions from the exocrine pancreas. After conjugation to cholic acid, the degree of cholylsecretin absorption from the ileum of anesthetized rats was assessed from the increase in pancreatic secretions. A complication to the study was that intra-ileal infusion of native secretin caused a transient increase in the levels of pancreatic secretions. This was in contrast to the effects of intra-ileal infusion of cholylsecretin which did not cause this transient increase but, instead, gave rise to a delayed increase in pancreatic secretions which was sustained over several hours during which cholylsecretin was detected in plasma in high concentration by mass spectrometry. The pancreatic response to cholylsecretin was abolished by co-infusion of 50 mM taurocholate, employed to compete with the bile salt transporters, although a transient increase in pancreatic secretions similar to that caused by secretin was now generated. This was shown to arise from an action of taurocholate per se causing the release of endogenous secretin which is present in rat ileum. The authors, therefore, concluded that cholylsecretin had been absorbed from the rat ileum by uptake by bile salt transporters.  
 ST secretin cholic acid conjugate bile salt absorption ileum rat; cholylsecretin absorption bile salt transporter ileum  
 IT Pancreas  
     (absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)  
 IT Transport proteins  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
         (bile salt; absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)  
 IT Intestine  
     (ileum; absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)  
 IT Bile salts  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
         (transporter; absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)  
 IT Biological transport  
     (uptake; absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)

Search done by Noble Jarrell

IT 71-52-3, Bicarbonate, biological studies 709002-71-1  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (absorption of cholic acid-conjugated peptide hormone cholylsecretin  
 from the rat ileum in vivo)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Baker, R; Proc Soc Exp Biol Med 1960, V105, P521 HCAPLUS
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IT 709002-71-1

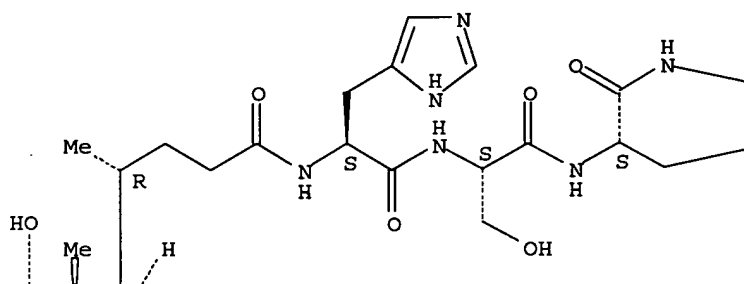
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (absorption of cholic acid-conjugated peptide hormone cholylsecretin  
 from the rat ileum in vivo)

RN 709002-71-1 HCAPLUS

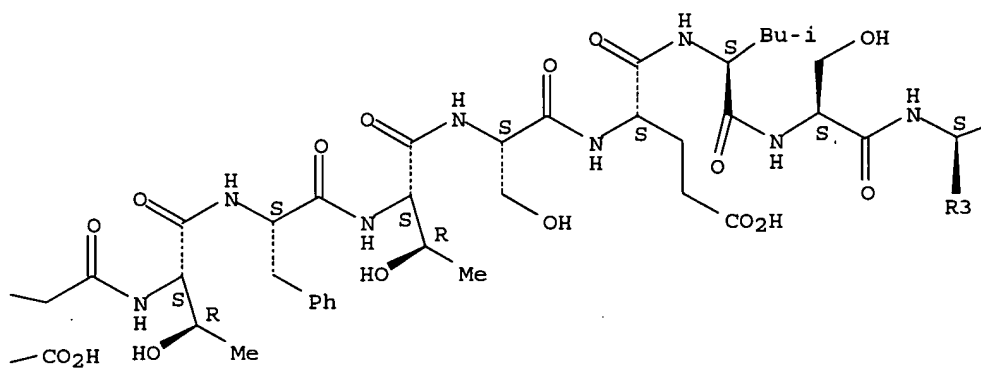
CN L-Valinamide, N-[(3 $\alpha$ , 5 $\beta$ , 7 $\alpha$ , 12 $\alpha$ )-3, 7, 12-trihydroxy-  
 24-oxocholan-24-yl]-L-histidyl-L-seryl-L- $\alpha$ -aspartylglycyl-L-threonyl-  
 L-phenylalanyl-L-threonyl-L-seryl-L- $\alpha$ -glutamyl-L-leucyl-L-seryl-L-  
 arginyl-L-leucyl-L-arginyl-L- $\alpha$ -glutamylglycyl-L-alanyl-L-arginyl-L-  
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 leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

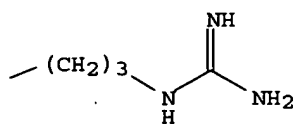
PAGE 1-A



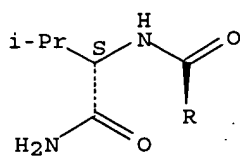
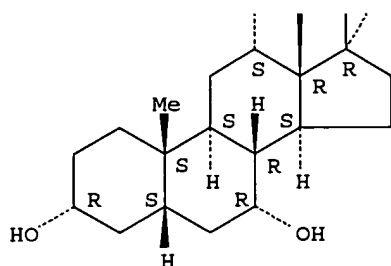
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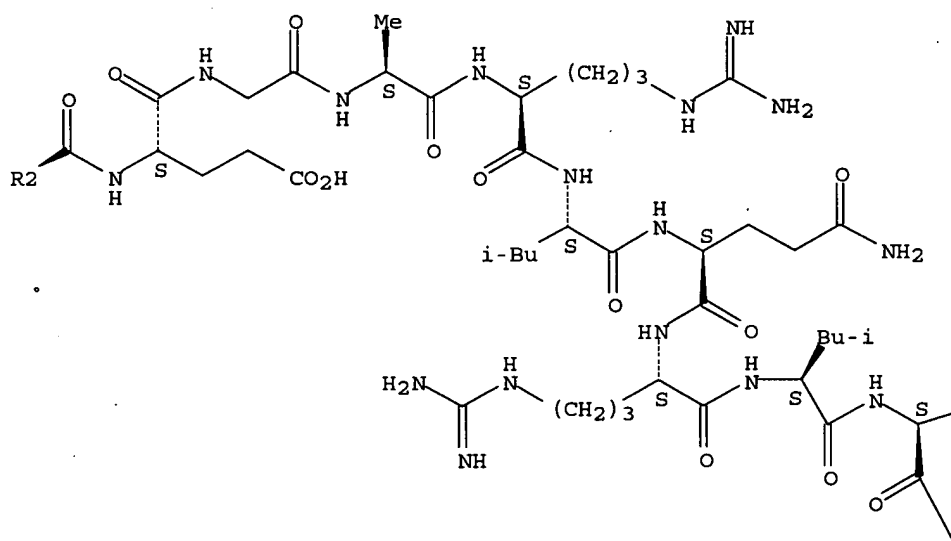
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PAGE 2-A



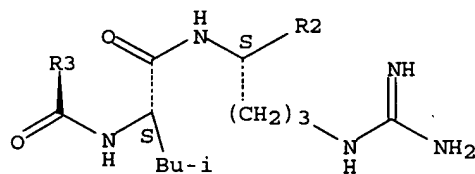
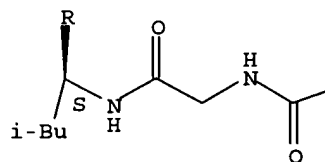
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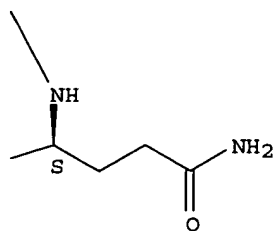
PAGE 3-B

Bu-i

PAGE 4-A



PAGE 4-B



L30 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2002:869795 HCAPLUS  
 DN 138:181158  
 ED Entered STN: 17 Nov 2002  
 TI Absorption of biologically active peptide hormones from the small intestine of rat  
 AU Wheeler, S.; McGinn, B. J.; Lucas, M. L.; Morrison, J. D.  
 CS University of Glasgow, Glasgow, G12 8QQ, UK  
 SO Acta Physiologica Scandinavica (2002), 176(3), 203-213  
 CODEN: APSCAX; ISSN: 0001-6772  
 PB Blackwell Science Ltd.  
 DT Journal  
 LA English  
 CC 2-6 (Mammalian Hormones)  
 AB Absorption of the 4, 10 and 34 amino acid forms of gastrin from the small intestine has been investigated in anesthetized rats. The method of assessment of successful absorption of the hormone into the systemic circulation was when the amount of acid secreted by the stomach over consecutive 15-min periods was increased. When the natural hormones were infused into the ileum in a relatively high dose, there was no increase in gastric acid secretion, indicating that they had not been absorbed. Each of the forms of gastrin was conjugated at the free N-terminus to the carboxyl group of cholic acid. Subsequent infusion of the conjugated form of gastrin into the ileum, this time in relatively low doses, resulted in substantial and prolonged increases in gastric acid secretion, indicating that these hormones had been successfully absorbed. In addition, conjugation of the 10 and 34 amino acid forms of gastrin with cholic acid was shown to increase markedly the potency in evoking an increase in gastric acid secretion in response to i.v. injection of the hormone. Absorption of the gastrin conjugates was specific to the ileum thus indicating that they had been absorbed through the bile salt transporters.  
 ST gastrin isoform absorption small intestine rat  
 IT Transport proteins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (bile salt; absorption of biol. active peptide hormones from ileum of rat indicates absorption through bile salt transporters)  
 IT Intestine  
 (ileum; absorption of biol. active peptide hormones from the small intestine of rat)  
 IT Gastric acid  
 (secretion; absorption of biol. active peptide hormones from the small intestine of rat)  
 IT Circulation  
 (systemic; absorption of biol. active peptide hormones from the small intestine of rat)  
 IT Bile salts  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (transporter; absorption of biol. active peptide hormones from ileum of rat indicates absorption through bile salt transporters)  
 IT Biological transport  
 (uptake; absorption of biol. active peptide hormones from the small intestine of rat)  
 IT 1947-37-1, 4-7-Cholecystokinin-7 (swine) 18828-47-2 171511-54-9  
 324753-46-0 496946-81-7 499210-69-4 499210-82-1  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (absorption of biol. active peptide hormones from the small intestine of rat)  
 IT 81-25-4, Cholic acid  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (conjugate; absorption of biol. active peptide hormones from the small intestine of rat)  
 RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
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IT 171511-54-9

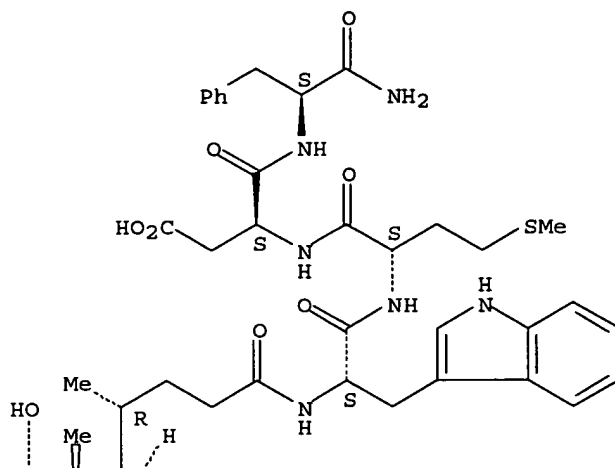
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(absorption of biol. active peptide hormones from the small intestine  
of rat)

RN 171511-54-9 HCAPLUS

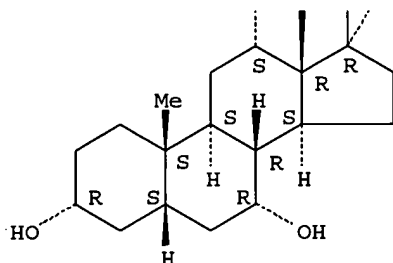
CN L-Phenylalaninamide, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-  
trihydroxy-24-oxocholan-24-yl]-L-tryptophyl-L-methionyl-L- $\alpha$ -aspartyl-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 2-A



L30 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2001:101167 HCAPLUS  
 DN 134:168315  
 ED Entered STN: 09 Feb 2001  
 TI Enhancement of bioavailability of peptides with bile salts  
 IN Morrison, James Duncan; Lucas, Michael Leslie;  
 Wheeler, Sarah  
 PA The University Court of the University of Glasgow, UK  
 SO PCT Int. Appl., 28 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J  
 CC 63-5 (Pharmaceuticals)  
 Section cross-reference(s): 1  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001009163	A2	20010208	WO 2000-GB2903	20000728
	WO 2001009163	A3	20010907		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

Search done by Noble Jarrell

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

GB 2355009 A1 20010411 GB 1999-17793 19990730  
 AU 2000061739 A5 20010219 AU 2000-61739 20000728  
 EP 1228093 A2 20020807 EP 2000-948177 20000728  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL  
 PRAI GB 1999-17793 A 19990730  
 WO 2000-GB2903 W 20000728

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001009163	ICM	C07J
WO 2001009163	ECLA	A61K047/48H4; C07K014/47; C07K014/575; C07K014/595
GB 2355009	ECLA	A61K047/48H4; C07K014/47; C07K014/575; C07K014/595
OS	MARPAT 134:168315	
AB	The present invention relates to improving and/or increasing the bioavailability of a biol. active substance, such as a peptide. In particular the present invention relates to the conjugation of the biol. active substance to a bile acid. The conjugated biol. active substance is suitable particularly for oral or parental administration. Ileal administration of 600µg/kg gastrin tetrapeptide conjugated to cholate resulted in a significant mean increase in gastric acid secretion of 1.84 µmol over a 3 h collection period, while no increase in acid secretion was noticed by administration of tetragastrin alone or with sep. cholate.	
ST	bioavailability enhancement peptide bile salt	
IT	Immunoglobulins RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (A; enhancement of bioavailability of peptides with bile salts)	
IT	Immunoglobulins RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (D; enhancement of bioavailability of peptides with bile salts)	
IT	Immunoglobulins RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (E; enhancement of bioavailability of peptides with bile salts)	
IT	Immunoglobulins RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (G; enhancement of bioavailability of peptides with bile salts)	
IT	Immunoglobulins RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (M; enhancement of bioavailability of peptides with bile salts)	
IT	Chemotherapy (agents; enhancement of bioavailability of peptides with bile salts)	
IT	Adrenoceptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; enhancement of bioavailability of peptides with bile salts)	
IT	Anemia (disease) (antianemic factors; enhancement of bioavailability of peptides with bile salts)	

- IT Peptides, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
 (conjugates; enhancement of bioavailability of peptides with bile salts)
- IT Adrenoceptor agonists  
 Adrenoceptor antagonists  
 Analgesics  
 Anesthetics  
 Anti-inflammatory agents  
 Antianginal agents  
 Antiarrhythmics  
 Antibacterial agents  
 Anticoagulants  
 Anticonvulsants  
 Antidepressants  
 Antihistamines  
 Antiparkinsonian agents  
 Antipsychotics  
 Antiviral agents  
 Anxiolytics  
 Cardiotonics  
 Diuretics  
 Drug bioavailability  
 Fungicides  
 Hypnotics and Sedatives  
 Hypolipemic agents  
 Muscarinic agonists  
 Muscarinic antagonists  
 Nicotinic antagonists  
 Parasitocides  
 Permeation enhancers  
 Stomach  
 Vasodilators  
 (enhancement of bioavailability of peptides with bile salts)
- IT Peptides, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (enhancement of bioavailability of peptides with bile salts)
- IT Antibodies  
 Blood-coagulation factors  
 Ferritins  
 Glycoproteins, general, biological studies  
 Hemoglobins  
 Interferons  
 Oligonucleotides  
 Opioids  
 Polynucleotides  
 Polysaccharides, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (enhancement of bioavailability of peptides with bile salts)
- IT Bile acids  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (enhancement of bioavailability of peptides with bile salts)
- IT Bile salts  
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (enhancement of bioavailability of peptides with bile salts)
- IT Gastrointestinal motility  
 (gastric, drugs for treatment of; enhancement of bioavailability of

- peptides with bile salts)
- IT Drug delivery systems  
(oral; enhancement of bioavailability of peptides with bile salts)
- IT Drug delivery systems  
(parenterals; enhancement of bioavailability of peptides with bile salts)
- IT Antiulcer agents  
(peptic; enhancement of bioavailability of peptides with bile salts)
- IT Neuropeptides  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(transmitters; enhancement of bioavailability of peptides with bile salts)
- IT 9001-08-5D, inhibitor  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(anticholinesterase; enhancement of bioavailability of peptides with bile salts)
- IT 50-56-6, Oxytocin, biological studies 1393-25-5, Secretin 8001-27-2, Hirudin 9001-05-2, Catalase 9001-27-8, Factor viii 9001-28-9, Factor IX 9002-60-2, Acth, biological studies 9002-61-3, Chorionic gonadotropin 9002-64-6, Parathyroid hormone 9002-67-9, Luteinizing hormone 9002-68-0, Follicle stimulating hormone 9002-71-5, Thyroid stimulating hormone 9002-72-6, Somatotropin 9002-76-0, Gastrin 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin 9007-43-6, Cytochrome c, biological studies 9007-92-5, Glucagon, biological studies 9011-97-6, Cholecystokinin 9015-71-8, Corticotropin releasing hormone 9015-94-5, Renin, biological studies 9034-39-3, Growth hormone releasing hormone 9034-40-6, Gonadotropin releasing hormone 9038-70-4, Somatomedin 9039-53-6, Urokinase 9041-90-1, Angiotensin I 9054-89-1, Superoxide dismutase 9087-70-1, Aprotinin 11000-17-2, Antidiuretic hormone 11096-26-7, Erythropoietin 11128-99-7, Angiotensin II 24305-27-9, Thyrotropin releasing hormone 51110-01-1, Somatostatin 57285-09-3, Inhibin 59392-49-3, Gastric inhibitory peptide 67763-96-6, Igf1 67763-97-7, Igf2 80043-53-4, Gastrinreleasing peptide 85637-73-6, Atrial natriuretic hormone 89750-14-1, Glucagon-like peptide I 119418-04-1, Galanin 139639-23-9, Tissue plasminogen activator  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(enhancement of bioavailability of peptides with bile salts)
- IT 79-14-1D, Glycolic acid, salts 81-24-3D, Taurocholic acid, salts 81-25-4, Cholic acid 83-44-3D, Deoxycholic acid, salts 128-13-2D, Ursodeoxycholic acid, salts 360-65-6D, Glycodeoxycholic acid, salts 474-25-9D, Chenodeoxycholic acid, salts 474-74-8D, Glycolithocholic acid, salts 516-35-8D, Taurochenodeoxycholic acid, salts 516-50-7D, Taurodeoxycholic acid, salts 516-90-5D, TAurolithocholic acid, salts 640-79-9D, Glycochenodeoxycholic acid, salts 14605-22-2D, Tauroursodeoxycholic acid, salts 63948-32-3 64480-66-6D, Glycoursodeoxycholic acid, salts 83381-47-9, Gastrin-34 I (rat) 171511-54-9 324753-46-0 325142-35-6  
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(enhancement of bioavailability of peptides with bile salts)
- IT 9003-99-0, Peroxidase  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(horseradish; enhancement of bioavailability of peptides with bile salts)
- IT 9002-10-2, Tyrosinase  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mushroom; enhancement of bioavailability of peptides with bile salts)

IT 9035-81-8, Trypsin inhibitor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(soy bean; enhancement of bioavailability of peptides with bile salts)

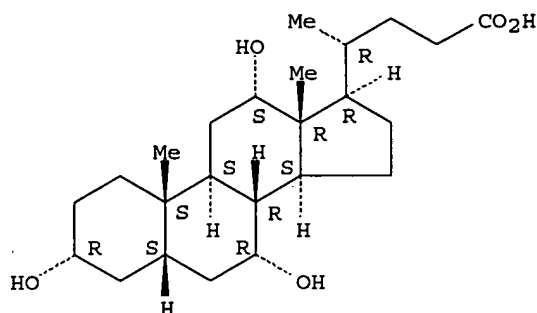
IT 81-25-4, Cholic acid

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(enhancement of bioavailability of peptides with bile salts)

RN 81-25-4 HCAPLUS

CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$  a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L30 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1991:580392 HCAPLUS

DN 115:180392

ED Entered STN: 01 Nov 1991

TI The effect of sodium deoxycholate and other surfactants on the mucosal surface pH in proximal jejunum of rat

AU McKie, A. T.; Stewart, W.; Lucas, M. L.

CS Inst. Physiol., Glasgow Univ., Glasgow, G12 8QQ, UK

SO Naunyn-Schmiedeberg's Archives of Pharmacology (1991), 343(6), 659-64

CODEN: NSAPCC; ISSN: 0028-1298

DT Journal

LA English

CC 13-7 (Mammalian Biochemistry)

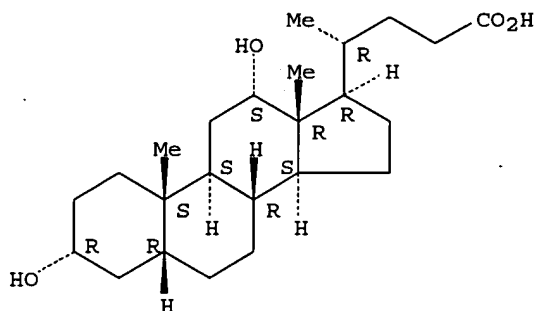
AB The mucosal surface pH (acid microclimate) and nucleotide levels of rat proximal jejunum were measured in vivo under various conditions which included exposure to pharmacol. agents and to surfactants. Mucosal surface pH was unaffected by sodium nitroprusside, A 23187, and amiloride, as was mucosal cGMP content, although amiloride and A 23187 reduced cAMP content. In contrast, surfactants elevated the pH of the mucosal surface significantly: control value 6.23; Lubrol PX 0.8% (volume/volume) 6.98 sodium deoxycholate 2 mM 6.67; Triton X 100 0.5% (volume/volume) 7.41. No significant changes in cGMP levels were noted after surfactant treatment, although deoxycholate and Triton X 100 reduced cAMP levels. The ability of higher concns. of surfactant to elevate the mucosal surface pH beyond neutrality to values similar to plasma pH contrasts with the action of Escherichia coli heat-stable (STa) enterotoxin, which at high concns. could not elevate the mucosal surface pH beyond neutrality. Consistent with the known effects on tight junction permeability, surfactants may act by allowing plasma-like subepithelial fluid to neutralize the microclimate.

ST jejunum mucosa pH surfactant; cAMP jejunum mucosa pH surfactant; cGMP jejunum mucosa pH surfactant

IT Surfactants

- (proximal jejunum mucosal surface pH response to, ion movements and cyclic nucleotides in relation to)
- IT Intestine  
(jejunum, proximal, mucosa, surface pH of, surfactants effect on, ion movements and cyclic nucleotides in relation to)
- IT 7440-23-5, Sodium, biological studies  
RL: BIOL (Biological study)  
(hydrogen ion exchange with, in jejunum mucosa, effect of surfactant on surface pH in relation to)
- IT 60-92-4, CAMP 7665-99-8, CGMP  
RL: BIOL (Biological study)  
(of jejunum mucosa, surfactants effect on, mucosal surface pH in relation to)
- IT 302-95-4, Sodium deoxycholate 577-11-7 9002-92-0, Lubrol PX  
9002-93-1, Triton X-100  
RL: BIOL (Biological study)  
(proximal jejunum mucosal surface pH response to, ion movements and cyclic nucleotides in relation to)
- IT 12408-02-5, Hydrogen ion, biological studies  
RL: BIOL (Biological study)  
(sodium exchange with, in jejunum mucosa, effect of surfactant on surface pH in relation to)
- IT 7440-70-2, Calcium, biological studies  
RL: BIOL (Biological study)  
(transport of, by jejunum mucosa, surfactants effect on surface pH and cyclic nucleotides in relation to)
- IT 302-95-4, Sodium deoxycholate  
RL: BIOL (Biological study)  
(proximal jejunum mucosal surface pH response to, ion movements and cyclic nucleotides in relation to)
- RN 302-95-4 HCAPLUS
- CN Cholan-24-oic acid, 3,12-dihydroxy-, monosodium salt,  
(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na

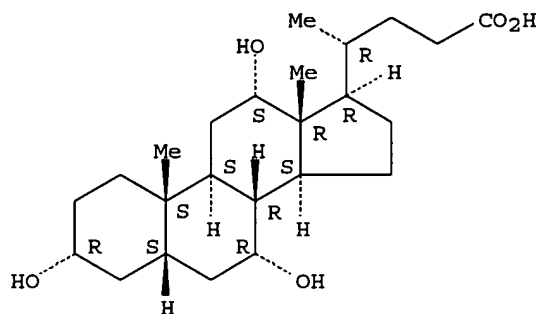
L30 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 1984:32553 HCAPLUS  
DN 100:32553  
ED Entered STN: 12 May 1984  
TI The effect of deoxycholate on intestinal surface pH and  
5-methyltetrahydropteroylglutamate absorption in the rat proximal jejunum  
in vitro  
AU Blair, John A.; Hilburn, Michael E.; Lucas, Michael L.; Said,  
Hamid M.  
CS Dep. Chem., Univ. Aston, Birmingham, B4 7ET, UK  
SO Biochemical Society Transactions (1983), 11(2), 165-7

Search done by Noble Jarrell

CODEN: BCSTB5; ISSN: 0300-5127

DT Journal  
 LA English  
 CC 13-2 (Mammalian Biochemistry)  
 AB The effects of deoxycholate (0.01-10 mM) on rat proximal jejunum in vitro indicated that intestinal surface pH is a determinant of folate absorption.  
 ST intestine pH folate absorption deoxycholate  
 IT Bile acids  
 RL: BIOL (Biological study)  
 (folate absorption by intestinal jejunum response to, surface pH in relation to)  
 IT Intestine, metabolism  
 (proximal jejunum, folate absorption by, deoxycholate effect on, surface pH in relation to)  
 IT 59-30-3, biological studies 134-35-0  
 RL: BIOL (Biological study)  
 (absorption of, by proximal jejunum, deoxycholate effect on, surface pH in relation to)  
 IT 81-25-4 360-65-6  
 RL: BIOL (Biological study)  
 (folate absorption by intestinal jejunum response to, surface pH in relation to)  
 IT 83-44-3  
 RL: BIOL (Biological study)  
 (folate absorption by proximal jejunum response to, surface pH in relation to)  
 IT 81-25-4  
 RL: BIOL (Biological study)  
 (folate absorption by intestinal jejunum response to, surface pH in relation to)  
 RN 81-25-4 HCAPLUS  
 CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ -a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d all hitstr 140 tot

L40 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2002:537280 HCAPLUS  
 DN 138:85395  
 ED Entered STN: 19 Jul 2002  
 TI Participation of two members of the very long-chain acyl-CoA synthetase family in bile acid synthesis and recycling  
 AU Mihalik, Stephanie J.; Steinberg, Steven J.; Pei, Zhengtong; Park, Joseph; Kim, Do G.; Heinzer, Ann K.; Dacremont, Georges; Wanders, Ronald J. A.; Cuebas, Dean A.; Smith, Kirby D.; Watkins, Paul A.  
 CS Kennedy Krieger Institute and the Department of Pediatrics, Johns Hopkins

University School of Medicine, Baltimore, MD, 21205, USA

SO Journal of Biological Chemistry (2002), 277(27), 24771-24779  
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 7-2 (Enzymes)  
Section cross-reference(s): 3, 13

OS CASREACT 138:85395

AB Bile acids are synthesized de novo in the liver from cholesterol and conjugated to glycine or taurine via a complex series of reactions involving multiple organelles. Bile acids secreted into the small intestine are efficiently reabsorbed and reutilized. Activation by thioesterification to CoA is required at two points in bile acid metabolism. First, 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-5 $\beta$ -cholestanoic acid, the 27-carbon precursor of cholic acid, must be activated to its CoA derivative before side chain cleavage via peroxisomal  $\beta$ -oxidation. Second, reutilization of cholate and other C24 bile acids requires reactivation prior to re-conjugation. We reported previously that homolog 2 of very long-chain acyl-CoA synthetase (VLCS) can activate cholate. We now show that homolog 2 also activates chenodeoxycholate, the secondary bile acids deoxycholate and lithocholate, and 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-5 $\beta$ -cholestanoic acid. In contrast, VLCS activated 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-5 $\beta$ -cholestanoate, but did not utilize any of the C24 bile acids as substrates. We hypothesize that the primary function of homolog 2 is in the reactivation and recycling of C24 bile acids, whereas VLCS participates in the de novo synthesis pathway. Results of in situ hybridization, topog. orientation, and inhibition studies are consistent with the proposed roles of these enzymes in bile acid metabolism

ST very long chain acyl CoA synthetase bile acid recycling; mouse cDNA sequence bile acid CoA synthetase liver

IT Mus musculus  
(VLCS cDNA sequence; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

IT Bile acids  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(enzyme substrate specificity; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

IT Liver  
(hepatocyte, compartmentalized expression of VLCS; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

IT Molecular topology  
(membrane topol. of VLCS-H2; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

IT Protein sequences  
cDNA sequences  
(of VLCS of mouse liver; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

IT 114797-03-4P, Bile acid-CoA synthetase  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)  
(VLCS homolog 2; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

- IT 69403-06-1P, Very long-chain acyl-CoA synthetase  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)  
 (VLCS; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- IT 470737-50-9P  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)  
 (amino acid sequence; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- IT 83-44-3, Deoxycholic acid 434-13-9, Lithocholic acid 474-25-9, Chenodeoxycholic acid  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (enzyme substrate specificity; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- IT 547-98-8P  
 RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (enzyme substrate specificity; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- IT 5226-26-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (in preparation of bile acid precursor THCA; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- IT 3396-82-5, Sodium cyanide (Na(14CN))  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (in preparation of 14C-labeled trihydroxycholestanate; bile acid-CoA synthetase activity and cellular localization of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- IT 114416-41-0P 114443-04-8P 114443-05-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (in preparation of 14C-labeled trihydroxycholestanate; bile acid-CoA synthetase activity and cellular localization of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- IT 200385-45-1, GenBank AF033031  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (nucleotide sequence; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- IT 114416-40-9P  
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (14C-labeled enzyme substrate; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
- RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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IT 5226-26-6

RL: RCT (Reactant); RACT (Reactant or reagent)

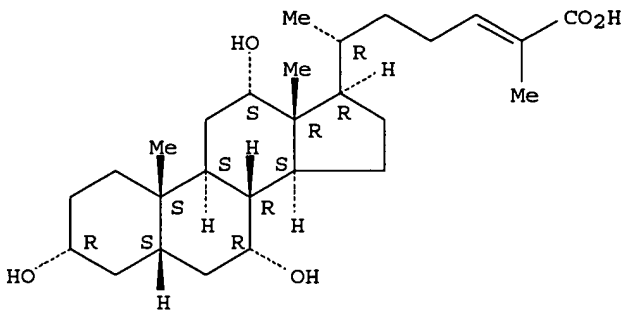
(in preparation of bile acid precursor THCA; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

RN 5226-26-6 HCAPLUS

CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-,  
(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



L40 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:508917 HCAPLUS

DN 133:140227

ED Entered STN: 27 Jul 2000

TI Method and compositions for lipidization of hydrophilic molecules

IN Shen, Wei-chiang; Wang, Jinghua  
 PA The University of Southern California, USA  
 SO U.S., 34 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K038-28  
 INCL 514003000  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1

## FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6093692	A	20000725	US 1997-936898	19970925 <--
PRAI	US 1996-77177P	P	19960926	<--	
	US 1997-49499P	P	19970613	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6093692	ICM	A61K038-28
	INCL	514003000
US 6093692	NCL	514/003.000; 514/002.000; 514/009.000; 514/019.000; 514/023.000; 530/300.000; 530/303.000; 530/307.000; 530/315.000; 530/317.000; 530/331.000; 530/333.000; 530/350.000
	ECLA	A61K047/48H4 <--

OS MARPAT 133:140227

AB Fatty acid derivs. of disulfide-containing compds. (for example, disulfide-containing peptides or proteins) comprising fatty acid-conjugated products with a disulfide linkage are employed for delivery of the compds. to mammalian cells. This modification markedly increases the absorption of the compds. by mammalian cells relative to the rate of absorption of the unconjugated compds., as well as prolonging blood and tissue retention of the compds. Moreover, the disulfide linkage in the conjugate is quite labile in vivo and thus facilitates intracellular or extracellular release of the intact compds. from the fatty acid moieties. N-palmityl-2-pyridyldithiocysteine was prepared and reacted with Bowman-Birk inhibitor (BBI) to obtain a palmityl disulfide conjugate of BBI. When the conjugate was incubated with colon carcinoma cells (Caco-2) in serum-free medium, the uptake of the conjugate was higher than that of BBI.

ST fatty acid disulfide protein conjugate bioavailability

IT Antisense oligonucleotides

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(complementary to mRNA of monoamine oxidase B, palmitylated;  
 conjugates of hydrophilic mols. with fatty acid or steroid  
 disulfide derivs. for improving their bioavailabilities)

IT Drug bioavailability

## Drug delivery systems

(conjugates of hydrophilic mols. with fatty acid or steroid  
 disulfide derivs. for improving their bioavailabilities)

IT Amino acids, biological studies

Carbohydrates, biological studies

Nucleosides, biological studies

Nucleotides, biological studies

Oligonucleotides

Peptides, biological studies

Proteins, general, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(conjugates with fatty acid disulfide derivs.;

conjugates of hydrophilic mols. with fatty acid or steroid  
 disulfide derivs. for improving their bioavailabilities)

IT Fatty acids, biological studies

Steroids, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (disulfide derivs., conjugates with proteins;  
conjugates of hydrophilic mols. with fatty acid or steroid  
disulfide derivs. for improving their bioavailabilities)
- IT Biological transport  
(drug; conjugates of hydrophilic mols. with fatty acid or  
steroid disulfide derivs. for improving their bioavailabilities)
- IT Drug delivery systems  
(liposomes; conjugates of hydrophilic mols. with fatty acid  
or steroid disulfide derivs. for improving their bioavailabilities)
- IT 16679-58-6DP, Desmopressin, fatty acid disulfide conjugates  
37330-34-ODP, Bowman-Birk inhibitor, oleyl disulfide conjugate  
37330-34-ODP, Bowman-Birk inhibitor, reaction product with  
N-succinimidyl-3-(2-pyridyldithio)propionate and N-Palmityl-2-  
pyridyldithiocysteine 171735-25-4DP, reaction products with proteins  
254453-83-3P 286365-28-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(conjugates of hydrophilic mols. with fatty acid or steroid  
disulfide derivs. for improving their bioavailabilities)
- IT 285981-92-2P 285981-94-4P  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(conjugates of hydrophilic mols. with fatty acid or steroid  
disulfide derivs. for improving their bioavailabilities)
- IT 57-11-4D, Stearic acid, disulfide derivs., conjugates with  
proteins 81-25-4D, disulfide derivs., conjugates with  
proteins 83-44-3D, disulfide derivs., conjugates with  
proteins 112-80-1D, Oleic acid, disulfide derivs., conjugates  
with proteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(conjugates of hydrophilic mols. with fatty acid or steroid  
disulfide derivs. for improving their bioavailabilities)
- IT 9003-99-ODP, Peroxidase, reaction product with N-succinimidyl-3-(2-  
pyridyldithio)propionate and N-Palmityl-2-pyridyldithiocysteine  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(horseradish; conjugates of hydrophilic mols. with fatty acid  
or steroid disulfide derivs. for improving their bioavailabilities)
- IT 9003-99-0, Peroxidase  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(horseradish; preparation of conjugates of hydrophilic mols. with  
fatty acid or steroid disulfide derivs. for improving their  
bioavailabilities)
- IT 52-90-4, L-Cysteine, reactions 83-44-3 1200-22-2, Lipoic acid  
2127-03-9, 2,2'-Dithiobis(pyridine) 6066-82-6, N-Hydroxysuccinimide  
14464-31-4 16679-58-6, Desmopressin 37330-34-0, Bowman-Birk inhibitor  
47931-85-1, Salmon calcitonin 59277-89-3, Acyclovir 68181-17-9, SPDP  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of conjugates of hydrophilic mols. with fatty acid or  
steroid disulfide derivs. for improving their bioavailabilities)
- IT 25596-79-6P, Calcitonin (salmon reduced) 37330-34-ODP, Bowman-Birk  
inhibitor, reaction product with N-succinimidyl-3-(2-  
pyridyldithio)propionate 88442-68-6P 119364-41-9P 171735-25-4P  
174069-00-2P 177902-84-0P 285981-91-1P 285981-93-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation of conjugates of hydrophilic mols. with fatty acid or  
steroid disulfide derivs. for improving their bioavailabilities)

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IT 285981-92-2P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

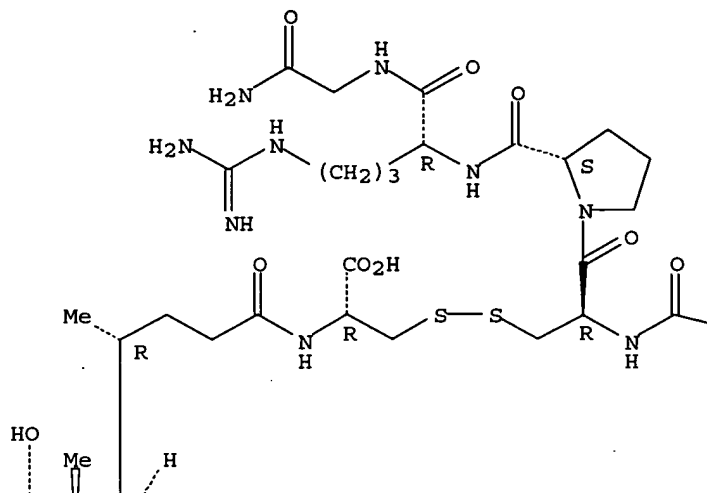
(conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

RN 285981-92-2 HCAPLUS

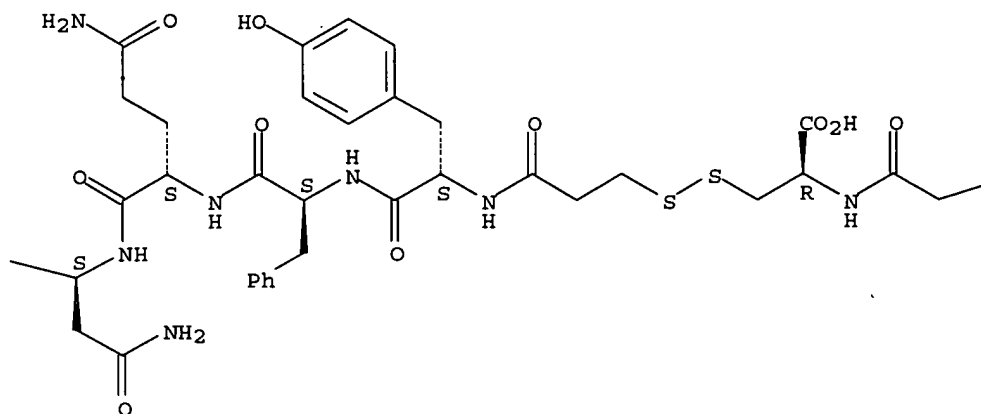
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-phenylalanyl-L-glutaminy-L-asparaginy-L-cysteinyl-L-prolyl-D-arginyl-, bis(disulfide) with N-[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]-L-cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

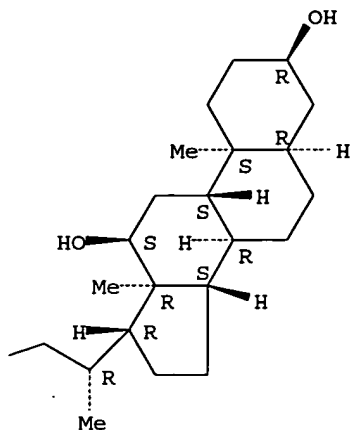
PAGE 1-A



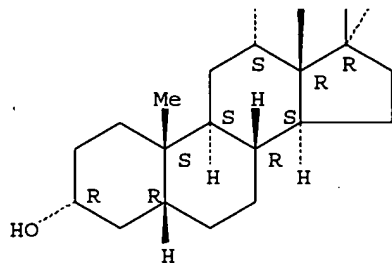
PAGE 1-B



PAGE 1-C

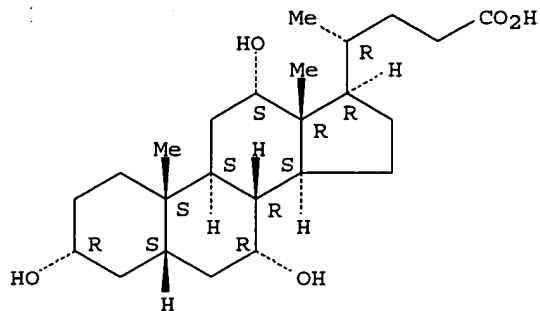


PAGE 2-A



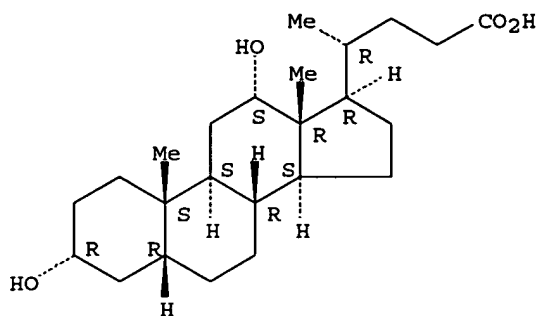
IT 81-25-4D, disulfide derivs., conjugates with proteins  
 83-44-3D, disulfide derivs., conjugates with proteins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (conjugates of hydrophilic mols. with fatty acid or steroid  
 disulfide derivs. for improving their bioavailabilities)  
 RN 81-25-4 HCAPLUS  
 CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ .alph  
 a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



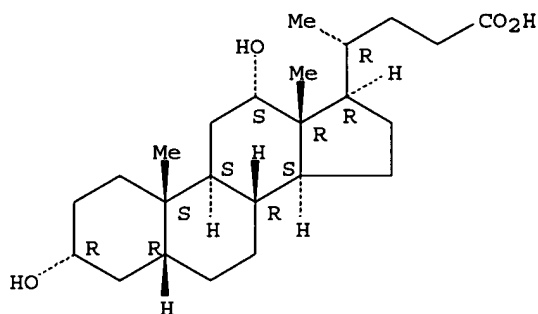
RN 83-44-3 HCAPLUS  
 CN Cholan-24-oic acid, 3,12-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



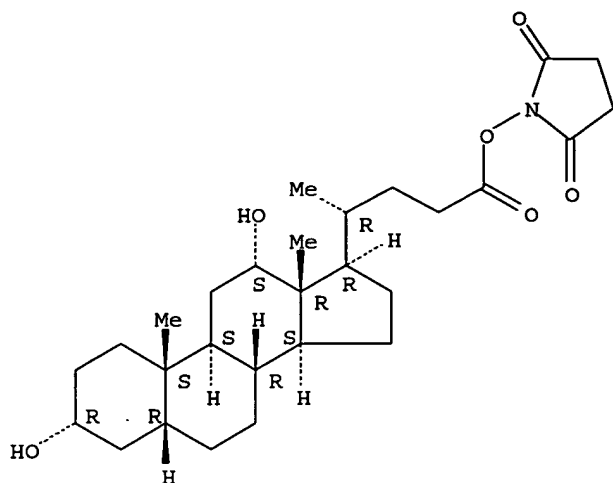
IT 83-44-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of conjugates of hydrophilic mols. with fatty acid or  
 steroid disulfide derivs. for improving their bioavailabilities)  
 RN 83-44-3 HCAPLUS  
 CN Cholan-24-oic acid, 3,12-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



IT 174069-00-2P 285981-91-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of conjugates of hydrophilic mols. with fatty acid or  
 steroid disulfide derivs. for improving their bioavailabilities)  
 RN 174069-00-2 HCAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[[[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-  
 oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

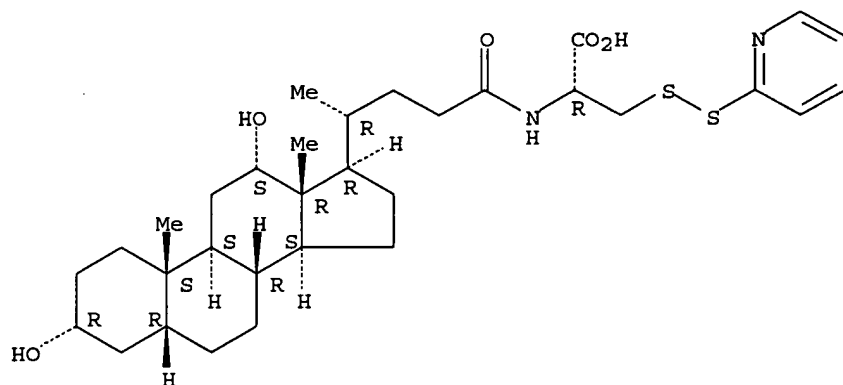
Absolute stereochemistry.



RN 285981-91-1 HCAPLUS

CN L-Alanine, N-[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]-3-(2-pyridinyldithio)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:10612 HCAPLUS

DN 132:73648

ED Entered STN: 06 Jan 2000

TI Lipophilic insulin derivatives soluble at physiological pH with prolonged serum half-lives and biological activity

IN Havelund, Svend; Halstrom, John; Jonassen, Ib; Andersen, Asser Sloth; Markussen, Jan

PA Novo Nordisk A/S, Den.

SO U.S., 47 pp., Cont.-in-part of U.S. 5,750,497.

CODEN: USXXAM

DT Patent

LA English

IC C07K014-62; A61K038-28

INCL 514003000

CC 1-10 (Pharmacology)

Section cross-reference(s): 2

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Search done by Noble Jarrell

PI	US 6011007	A	20000104	US 1997-975365	19971120 <--
	ZA 9407187	A	19950317	ZA 1994-7187	19940916 <--
	JP 2000060556	A2	20000229	JP 1999-221632	19940916 <--
	EP 1132404	A2	20010912	EP 2001-112992	19940916 <--
	EP 1132404	A3	20020327		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT				
	JP 2002308899	A2	20021023	JP 2001-385921	19940916 <--
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	EP 1994-926816	A3	19940916	<--	
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	US 1997-975365	A3	19971120	<--	
	US 1999-398365	A1	19990917	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
US 6011007	IC	C07K014-62IC	A61K038-28
	INCL	514003000	
US 6011007	NCL	514/003.000; 514/866.000; 530/303.000; 530/304.000	
	ECLA	C07K014/62	<--
EP 1132404	ECLA	C07K014/62	<--
US 5750497	NCL	514/003.000; 514/866.000; 530/304.000	
	ECLA	C07K014/62	<--
US 6869930	NCL	514/003.000; 514/866.000; 530/304.000	
	ECLA	C07K014/62	<--
US 2004110664	NCL	514/003.000	
	ECLA	C07K014/62	<--

OS MARPAT 132:73648

AB Human insulin derivs. with improved solubility at physiol. pH and that retain biol. activity for longer than wild-type human insulin are described. The insulins are substituted at positions A21 and B3 with either being any amino acid except lysine, arginine, or cysteine. The phenylalanine at B1 may be deleted and the amino acid at position B30 may be deleted or substituted by any amino acid except lysine, arginine, or cysteine or by another amino acid that is lipophilic having a C10-24 side chain. If B30 is deleted or substituted, lysineB29 is modified by a carboxylic acid connected to the ε-amino group. When B30 is threonine or alanine and A21 and B3 are both asparagine, and phenylalanineB1 is present, then the insulin derivative is always present as a Zn<sub>2</sub> complex.

ST human insulin sequence acylation diabetes pharmaceutical; lipophilic insulin deriv antidiabetic

IT Carboxylic acids, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(C5, insulins modified with; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Solubility

(at physiol. pH; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Carboxylic acids, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(dicarboxylic, C<6, insulin modification by; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT cDNA sequences

(for insulin analogs of human; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Drug delivery systems

(injections, insulin; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Antidiabetic agents

- (insulin analogs as; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT Acetyl group  
Formyl group  
(insulin derivs. containing; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT Fatty acids, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(insulin derivs. containing; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT Protein sequences  
(lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT Lipophilicity  
(of insulin derivs.; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT Plasmids  
(pAK-series and pKFN1627 and pEA-series; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT Functional groups  
(propionyl, insulin derivs. containing; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT 14464-31-4 69888-86-4 88404-23-3 104943-24-0 165893-02-7  
165893-03-8 168986-19-4 168986-20-7 169142-69-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylation of insulin derivs. using; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT 169148-55-4DP, zinc complexes 169148-56-5DP, zinc complexes  
169148-57-6P 169148-58-7P 169148-59-8P 169148-60-1P 169148-61-2DP,  
zinc complexes 169148-62-3DP, zinc complexes 169148-63-4P  
169148-64-5P 169148-65-6P 169148-66-7P 169148-67-8P 169148-68-9P  
169148-69-0P 169148-70-3P 169148-71-4P 169148-72-5DP, zinc complexes  
169148-73-6P 169148-74-7DP, zinc complexes 169148-75-8DP, zinc  
complexes 169535-16-4P 169535-18-6P 169535-20-0P 169535-22-2P  
169535-24-4P 169535-26-6P 169535-28-8P 169535-30-2P 169535-32-4P  
169535-34-6P 169535-36-8P 169535-38-0P  
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT 11061-68-0D, Insulin (human), amino acid-substituted, derivatized  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
- IT 51-49-0DP, conjugates with insulin 108-30-5DP,  
conjugates with insulin 110-15-6DP, Butanedioic acid,  
conjugates with insulin, preparation 143-07-7DP, Dodecanoic  
acid, conjugates with insulin, preparation 544-63-8DP,  
Tetradecanoic acid, conjugates with insulin, preparation  
638-53-9DP, Tridecanoic acid, conjugates with insulin  
7145-63-3DP, conjugates with insulin 7452-59-7DP,  
conjugates with insulin 7769-79-1DP, conjugates with  
insulin 14565-47-0DP, conjugates with insulin 17702-88-4DP,  
conjugates with insulin 22102-66-5DP, conjugates with  
insulin 35237-37-7DP, conjugates with insulin 68528-80-3DP,  
conjugates with insulin 104211-94-1DP,  
conjugates with insulin 141537-81-7DP, conjugates with  
insulin 158627-30-6DP, conjugates with insulin  
168986-14-9DP, conjugates with insulin 168986-15-0DP,  
conjugates with insulin 168986-16-1DP, conjugates with  
insulin  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(lipophilic insulin derivs. soluble at physiol. pH with prolonged serum

half-lives and biol. activity)

IT 23713-49-7DP, Zinc dication, complexes with insulin derivs., biological studies  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 169535-21-1P 169535-23-3P, DNA (Saccharomyces cerevisiae synthetic signal peptide LaC212spx3 fusion protein with synthetic peptide fusion protein with human insulin A chain [21-glycine] fusion protein with human insulin B-chain [3-aspartic acid]-specifying cDNA plus flanks)  
 169535-27-7P 169535-29-9P 169535-33-5P 169535-35-7P 169535-37-9P 169535-39-1P  
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (nucleotide sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 169535-17-5, DNA (Saccharomyces cerevisiae clone pAK188 synthetic signal peptide LaC212spx3 fusion protein with human clone pAK188 1-29-insulin B-chain fusion protein with synthetic clone pAK188 5-amino acid peptide fusion protein with human clone pAK188 insulin A-chain-specifying plus flanks) 169535-19-7 169535-25-5, DNA (Saccharomyces cerevisiae synthetic signal peptide LaC212spx3 fusion protein with human insulin A-chain [21-glycine] fusion protein with human insulin B-chain [3-aspartic acid]-specifying cDNA plus flanks)  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nucleotide sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 24424-99-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (protecting group; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 222586-86-9, 3: PN: US6011007 SEQID: 3 unclaimed DNA 222586-87-0, 4: PN: US6011007 SEQID: 4 unclaimed DNA 222586-88-1, 5: PN: US6011007 SEQID: 5 unclaimed DNA 222586-89-2, 6: PN: US6011007 SEQID: 6 unclaimed DNA 222586-90-5, 7: PN: US6011007 SEQID: 7 unclaimed DNA 222586-91-6, 8: PN: US6011007 SEQID: 8 unclaimed DNA 222586-92-7, 9: PN: US6011007 SEQID: 9 unclaimed DNA 222586-93-8 222586-94-9 222586-95-0 222586-96-1 222586-98-3 222587-00-0 222587-09-9  
 RL: PRP (Properties)  
 (unclaimed nucleotide sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 253597-47-6 253597-48-7  
 RL: PRP (Properties)  
 (unclaimed protein sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Anon; GB 1492997 1977 HCAPLUS
- (2) Anon; JP 5767548 1982
- (3) Anon; WO 9112817 1991 HCAPLUS
- (4) Anon; Prescription Products Guide 1992, P942
- (5) Brange And Langkjaer; Chemical Stability of Insulin Acta Pharm Nord 1992, V4(3), P149
- (6) Breddam; US 4645740 1987 HCAPLUS
- (7) Doerge; Wilson and Gisvold's textbook of organic medicinal and pharmaceutical chemistry 1982, P774
- (8) Foye, W; Principles of Medicinal Chemistry 1974, P563
- (9) Gammelhoft; Phys Rev 1984, V64, P1321
- (10) Grant; US 3823125 1974 HCAPLUS
- (11) Haas; US 3528960 1970 HCAPLUS
- (12) Kurtz; Diabetologia 1983, V25, P322 MEDLINE
- (13) Lindsay; US 3950517 1976 HCAPLUS
- (14) Lindsay And Shall; The Acetylation of Insulin Biochem 1991, V121, P737

- (15) Marble, A; Joslin's Diabetes Mellitus, 12th Edition 1985, P380
- (16) Markussen; US 5008241 1991 HCAPLUS
- (17) Markussen; Prot Eng 1987, V1, P205 HCAPLUS
- (18) Markussen; Prot Eng 1988, V2, P157 HCAPLUS
- (19) Mims Annual; Section 6d "Insulin Preparations" 1991
- (20) Mims Annual; Section 6d "Insulin Preparations" 1993
- (21) Panayotis; US 5208217 1993 HCAPLUS
- (22) Samuel; Clin Exp Immunol 1978, V33, P252 HCAPLUS
- (23) Schade; Excerpta Medica 1983, P7
- (24) Schlichtkrull, J; "Insulin Crystals" (Ejnar Munksgaard) 1958, P21
- (25) Smyth; US 3868356 1975 HCAPLUS

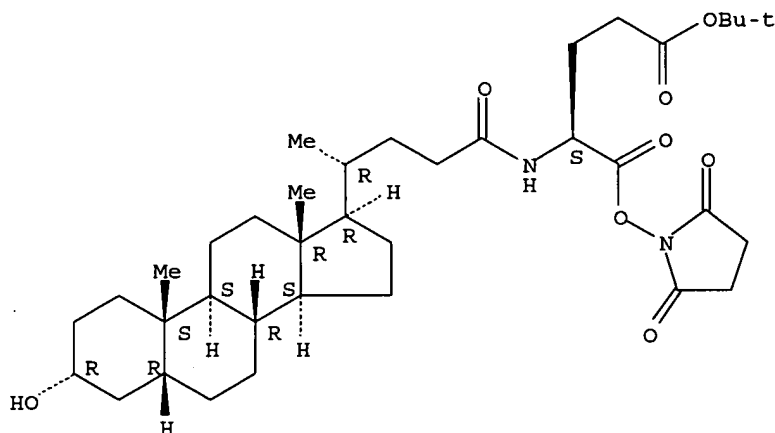
IT 168986-19-4

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acylation of insulin derivs. using; lipophilic insulin derivs. soluble at  
 physiol. pH with prolonged serum half-lives and biol. activity)

RN 168986-19-4 HCAPLUS

CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-[[ (3 $\alpha$ ,5 $\beta$ )-3-  
 hydroxy-24-oxocholan-24-yl]amino]-5-oxo-, 1,1-dimethylethyl ester, (4S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



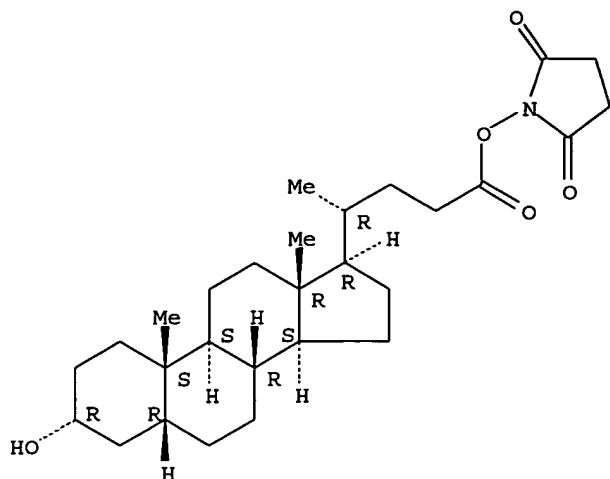
IT 104211-94-1DP, conjugates with insulin

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (lipophilic insulin derivs. soluble at physiol. pH with prolonged serum  
 half-lives and biol. activity)

RN 104211-94-1 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[[ (3 $\alpha$ ,5 $\beta$ )-3-hydroxy-24-oxocholan-24-  
 yl]oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1999:722480 HCAPLUS  
 DN 132:313463  
 ED Entered STN: 12 Nov 1999  
 TI Thermosensitive self-aggregates prepared from cholic acid-  
 conjugated amine-terminated poly(N-isopropylacrylamide) for drug  
 delivery  
 AU Kim, I. S.; Kim, S. H.  
 CS College of Pharmacy, Chosun University, Kwangju, 501-759, S. Korea  
 SO Proceedings of the International Symposium on Controlled Release of  
 Bioactive Materials (1999), 26th, 791-792  
 CODEN: PCRMEY; ISSN: 1022-0178  
 PB Controlled Release Society, Inc.  
 DT Journal  
 LA English  
 CC 63-5 (Pharmaceuticals)  
 AB Polymer micelles composed of cholic acid and amine-terminated  
 thermoresponsive poly(N-isopropylacrylamide) were prepared and showed  
 reversible thermal transition. Drug delivery systems using these  
 thermosensitive micelles can be used for the site-specific drug delivery  
 by modulating the temperature at the target site.  
 ST polyisopropylacrylamide nanoparticle micelle cholate drug delivery  
 IT Drug delivery systems  
 (nanoparticles, controlled-release; thermosensitive self-aggregates  
 prepared from cholic acid-conjugated amine-terminated  
 poly(N-isopropylacrylamide) for drug delivery)  
 IT Micelles  
 Self-association  
 (thermosensitive self-aggregates prepared from cholic acid-  
 conjugated amine-terminated poly(N-isopropylacrylamide) for  
 drug delivery)  
 IT 81-25-4DP, Cholic acid, reaction products with amine-terminated  
 poly(isopropylacrylamide) 25189-55-3DP, Poly(N-isopropylacrylamide),  
 amine-terminated, reaction products with cholic acid  
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (thermosensitive self-aggregates prepared from cholic acid-  
 conjugated amine-terminated poly(N-isopropylacrylamide) for  
 drug delivery)  
 IT 53-86-1, Indomethacin  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (thermosensitive self-aggregates prepared from cholic acid-

conjugated amine-terminated poly(N-isopropylacrylamide) for drug delivery)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

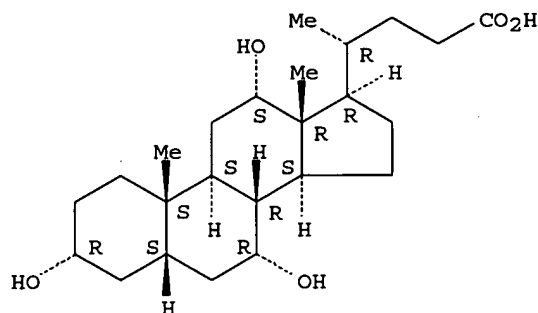
- (1) Anton, P; Makromol Chem 1993, V194, P1 HCAPLUS
- (2) Bae, Y; J Controlled Release 1989, V9, P271 HCAPLUS
- (3) Gao, Z; Macromolecules 1993, V26, P7353 HCAPLUS
- (4) Guenoun, P; Macromolecules 1996, V29, P3965 HCAPLUS
- (5) Xu, R; Macromolecules 1991, V24, P87 HCAPLUS

IT 81-25-4DP, Cholic acid, reaction products with amine-terminated poly(isopropylacrylamide)  
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(thermosensitive self-aggregates prepared from cholic acid-conjugated amine-terminated poly(N-isopropylacrylamide) for drug delivery)

RN 81-25-4 HCAPLUS

CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ .alph a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:708452 HCAPLUS

DN 131:314185

ED Entered STN: 05 Nov 1999

TI Active hedgehog protein conjugate, process for its production and use

IN Esswein, Angelika; Lang, Kurt; Rueger, Petra; Seytter, Tilmann

PA Roche Diagnostics G.m.b.H., Germany

SO Eur. Pat. Appl., 25 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM C07K014-47

ICA C07K019-00

CC 63-5 (Pharmaceuticals)

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 953576	A1	19991103	EP 1999-108032	19990423 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EP 953575	A1	19991103	EP 1998-107911	19980430 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NZ 335385	A	20000929	NZ 1999-335385	19990426 <--
	MX 9903976	A	20000630	MX 1999-3976	19990428 <--
	SG 80028	A1	20010417	SG 1999-2117	19990428 <--
	US 6468978	B1	20021022	US 1999-301199	19990428 <--
	CA 2269221	AA	19991030	CA 1999-2269221	19990429 <--

Search done by Noble Jarrell

NO 9902090	A	19991101	NO 1999-2090	19990429 <--
ZA 9903009	A	19991101	ZA 1999-3009	19990429 <--
CN 1233616	A	19991103	CN 1999-106302	19990429 <--
AU 9925009	A1	19991111	AU 1999-25009	19990429 <--
AU 719797	B2	20000518		
JP 2000053699	A2	20000222	JP 1999-125005	19990430 <--
JP 3433136	B2	20030804		
BR 9903169	A	20001017	BR 1999-3169	19990430 <--
US 2003139574	A1	20030724	US 2002-278060	20021021 <--
US 6818623	B2	20041116		
PRAI EP 1998-107911	A	19980430	<--	
EP 1998-116733	A	19980903	<--	
US 1999-301199	A1	19990428	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
EP 953576	ICM	C07K014-47	
	ICA	C07K019-00	
EP 953576	ECLA	C07K014/47	<--
EP 953575	ECLA	C07K014/47	<--
US 6468978	NCL	514/021.000; 514/012.000; 530/350.000; 530/408.000; 530/409.000; 530/410.000	
	ECLA	C07K014/47	<--
US 2003139574	NCL	514/021.000; 514/012.000; 530/350.000; 530/408.000; 530/409.000; 530/410.000	
	ECLA	C07K014/47	<--

AB A hedgehog conjugate is disclosed which is characterized in that it contains: (a) a polypeptide composed of 10 to 30 hydrophobic amino acids and/or amino acids which form transmembrane helixes and are pos. charged, (b) 1 to 4 aliphatic, saturated or unsatd. hydrocarbon residues with a chain length of 10 to 24 C atoms and with a hydrophobic action or (c) a hydrophobic thio compound covalently bound to a hedgehog protein and which has a several-fold increased activity and is suitable as a pharmaceutical agent.

ST hedgehog protein lipid conjugate drug

IT Polysaccharides, uses

RL: NUU (Other use, unclassified); USES (Uses)  
(acidic; active hedgehog protein conjugates for therapeutic use)

IT DNA sequences

Detergents

Drug delivery systems

Molecular cloning

Stabilizing agents

(active hedgehog protein conjugates for therapeutic use)

IT Primers (nucleic acid)

RL: PRP (Properties)

(active hedgehog protein conjugates for therapeutic use)

IT Alcohols, biological studies

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(alkyl, hedgehog protein conjugates; active hedgehog protein conjugates for therapeutic use)

IT Fatty acids, biological studies

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hedgehog protein conjugates; active hedgehog protein conjugates for therapeutic use)

IT Hedgehog protein

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)  
 (lipid conjugates; active hedgehog protein conjugates  
 for therapeutic use)

IT Dimerization  
 (of human sonic hedgehog protein; active hedgehog protein  
 conjugates for therapeutic use)

IT Hedgehog protein  
 RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP  
 (Preparation)  
 (sonic, cloning of human; active hedgehog protein conjugates  
 for therapeutic use)

IT 57-10-3DP, Palmitic acid, hedgehog protein conjugates  
 57-11-4DP, Stearic acid, hedgehog protein conjugates  
 60-33-3DP, Linoleic acid, hedgehog protein conjugates  
 112-80-1DP, Oleic acid, hedgehog protein conjugates  
 112-85-6DP, Behenic acid, hedgehog protein conjugates  
 143-07-7DP, Lauric acid, hedgehog protein conjugates  
 373-49-9DP, Palmitoleic acid, hedgehog protein conjugates  
 463-40-1DP, Linolenic acid, hedgehog protein conjugates  
 506-30-9DP, Arachidic acid, hedgehog protein conjugates  
 506-32-1DP, Arachidonic acid, hedgehog protein conjugates  
 544-63-8DP, Myristic acid, hedgehog protein conjugates  
 1249-81-6DP, Thiocholesterol, hedgehog protein conjugates  
 RL: BAC (Biological activity or effector, except adverse); BPN  
 (Biosynthetic preparation); BSU (Biological study, unclassified); PRP  
 (Properties); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (active hedgehog protein conjugates for therapeutic use)

IT 145-63-1, Suramin 9005-49-6, Heparin, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (active hedgehog protein conjugates for therapeutic use)

IT 361-09-1, Sodium cholate 2281-11-0, Zwittergent 3-16  
 9002-93-1, Triton x 100 9005-65-6, Tween 80 14933-09-6, Zwittergent  
 3-14 41444-50-2, Octyl glucoside 75621-03-3, Chaps  
 RL: NUU (Other use, unclassified); PRP (Properties); USES (Uses)  
 (active hedgehog protein conjugates for therapeutic use)

IT 3867-67-2P 17450-31-6P 26227-65-6P 60988-34-3P 69205-88-5P  
 69205-89-6P 136911-91-6P 247900-73-8P 247900-74-9P  
 247900-75-0P 247900-76-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (active hedgehog protein conjugates for therapeutic use)

IT 1763-10-6, Palmitoyl-CoA  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (coupling agent; active hedgehog protein conjugates for  
 therapeutic use)

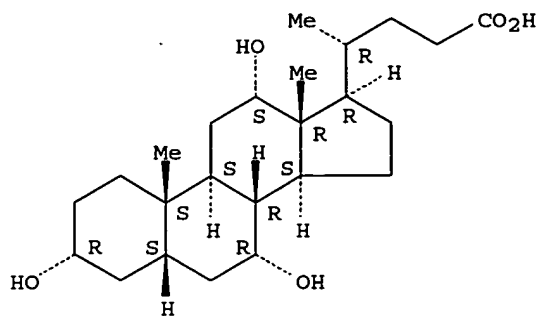
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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 (1) Beachy, P; WO 9830576 A 1998 HCAPLUS  
 (2) Farese, R; TRENDS IN GENETICS 1998, V14(3), P115 HCAPLUS  
 (3) Hammerschmidt, M; TRENDS IN GENETICS 1997, V13(1), P14 HCAPLUS  
 (4) Hancock; CELL 1990, V63, P133 HCAPLUS  
 (5) Harvard College; WO 9518856 A 1995 HCAPLUS  
 (6) Mohler; DEVELOPMENT 1992, V115, P957 HCAPLUS  
 (7) Porter; CELL 1996, V86, P21 HCAPLUS  
 (8) Porter; SCIENCE 1996, V274, P255 HCAPLUS

IT 361-09-1, Sodium cholate  
 RL: NUU (Other use, unclassified); PRP (Properties); USES (Uses)  
 (active hedgehog protein conjugates for therapeutic use)

RN 361-09-1 HCAPLUS

CN Cholan-24-oic acid, 3,7,12-trihydroxy-, monosodium salt,  
 (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )- (9CI) (CA INDEX NAME)

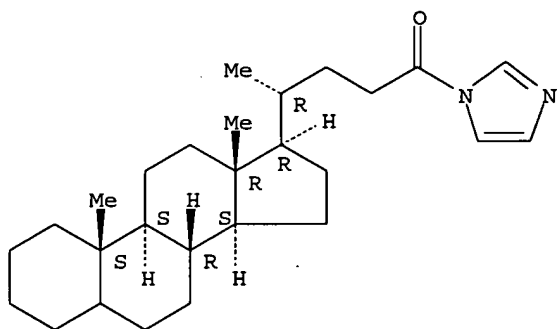
Absolute stereochemistry.



● Na

IT 247900-74-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (active hedgehog protein conjugates for therapeutic use)  
 RN 247900-74-9 HCAPLUS  
 CN 1H-Imidazole, 1-(24-oxocholan-24-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1998:208387 HCAPLUS  
 DN 128:286354  
 ED Entered STN: 13 Apr 1998  
 TI Methods and compositions for lipidization of hydrophilic molecules  
 IN Shen, Wei-Chiang; Wang, Jinghua  
 PA University of Southern California, USA; Shen, Wei-Chiang; Wang, Jinghua  
 SO PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9813007	A2	19980402	WO 1997-US17282	19970926 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,				

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UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,  
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,  
 GN, ML, MR, NE, SN, TD, TG

CA 2267179	AA	19980402	CA 1997-2267179	19970926 <--
AU 9745967	A1	19980417	AU 1997-45967	19970926 <--
AU 737865	B2	20010906		
CN 1235594	A	19991117	CN 1997-199191	19970926 <--
CN 1127477	B	20031112		
EP 1023316	A2	20000802	EP 1997-944483	19970926 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9712128	A	20001212	BR 1997-12128	19970926 <--
JP 2002515883	T2	20020528	JP 1998-515933	19970926 <--
NO 9901465	A	19990510	NO 1999-1465	19990325 <--
KR 2000048608	A	20000725	KR 1999-702543	19990325 <--
PRAI US 1996-721306	A	19960926	<--	
US 1997-49499P	P	19970613	<--	
US 1996-77177P	P	19960926	<--	
WO 1997-US17282	W	19970926	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 9813007	ICM	A61K	
WO 9813007	ECLA	A61K047/48H4	<--
OS	MARPAT 128:286354		
AB	Fatty acid derivs. of disulfide-containing compds. (for example, disulfide-containing peptides or proteins) comprising fatty acid-conjugated products with a disulfide linkage are employed for delivery of the compds. to mammalian cells. This modification markedly increases the absorption of the compds. by mammalian cells relative to the rate of absorption of the unconjugated compds., as well as prolonging blood and tissue retention of the compds. Moreover, the disulfide linkage in the conjugate is quite labile in vivo and thus facilitates intracellular or extracellular release of the intact compds. from the fatty acid moieties. N-palmitoyl-2-pyridyldithiocysteine was prepared and conjugated to BBI hydrophilic protein and its transport and biodistribution studied.		
ST	lipidization hydrophilic compd delivery; fatty acid deriv protein peptide delivery		
IT	Drug delivery systems (lipidization of hydrophilic mols. for peptide or protein delivery)		
IT	Disulfides RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (lipidization of hydrophilic mols. for peptide or protein delivery)		
IT	Drug delivery systems (liposomes; lipidization of hydrophilic mols. for peptide or protein delivery)		
IT	Proteins, general, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (reaction products with palmitoylpyridyldithiocysteine, lipidization of hydrophilic mols. for peptide or protein delivery)		
IT	Oligonucleotides Peptides, biological studies Proteins, specific or class RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (reaction products, with fatty acids; lipidization of hydrophilic mols. for peptide or protein delivery)		
IT	Fatty acids, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)		

(reaction products, with proteins and peptides; lipidization of hydrophilic mols. for peptide or protein delivery)

IT 112-80-1DP, Oleic acid, derivative, reaction products with peptides and proteins 1200-22-2DP, Lipoic acid, reaction products with acyclovir and palmitic acid derivative 9003-99-0DP, Peroxidase, reaction products with palmitic acid derivative 16679-58-6DP, Desmopressin, reaction products with palmitic acid derivative 47931-85-1DP, Salmon calcitonin, reaction products with palmitic acid derivative 59277-89-3DP, Acyclovir, reaction products with lipoic acid and palmitic acid derivative 171735-25-4DP, reaction products with peptides and proteins 174069-00-2DP, reaction products with palmitic acid derivative

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(lipidization of hydrophilic mols. for peptide or protein delivery)

IT 52-90-4, L-Cysteine, reactions 83-44-3, Deoxycholic acid 2127-03-9, Pyridine, 2,2'-Dithiobis- 6066-82-6, N-Hydroxysuccinimide 68181-17-9, SPDP

RL: RCT (Reactant); RACT (Reactant or reagent)

(lipidization of hydrophilic mols. for peptide or protein delivery)

IT 14464-31-4P, N-Hydroxysuccinimide palmitate 88442-68-6P 171735-25-4P 174069-00-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(lipidization of hydrophilic mols. for peptide or protein delivery)

IT 174069-00-2DP, reaction products with palmitic acid derivative

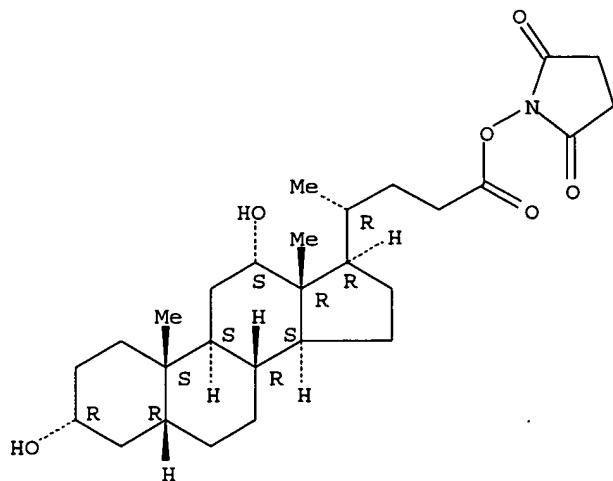
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(lipidization of hydrophilic mols. for peptide or protein delivery)

RN 174069-00-2 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[[[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 83-44-3, Deoxycholic acid

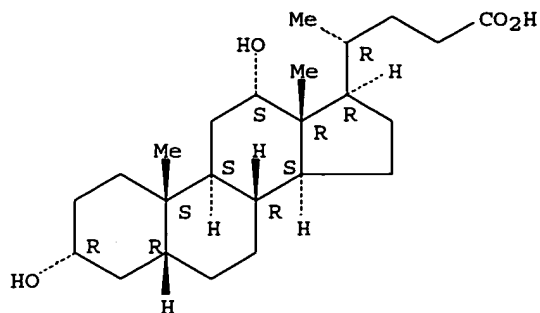
RL: RCT (Reactant); RACT (Reactant or reagent)

(lipidization of hydrophilic mols. for peptide or protein delivery)

RN 83-44-3 HCAPLUS

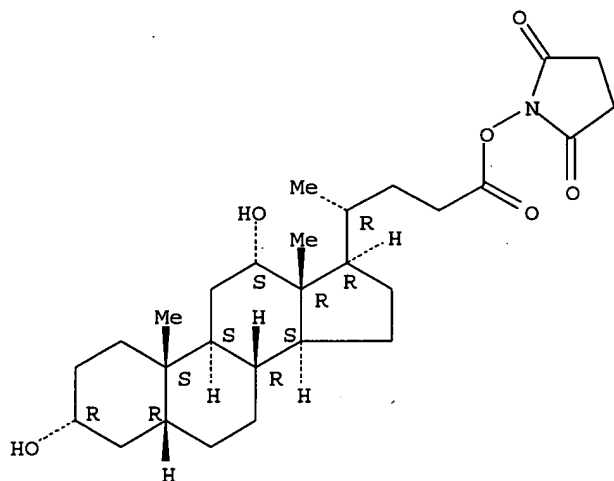
CN Cholan-24-oic acid, 3,12-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 174069-00-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (lipidization of hydrophilic mols. for peptide or protein delivery)  
 RN 174069-00-2 HCAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[[[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-  
 oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1997:463447 HCAPLUS  
 DN 127:99659  
 ED Entered STN: 24 Jul 1997  
 TI Oral peptide delivery using the intestinal bile acid transporter  
 AU Swaan, P. W.; Szoka, F. C., Jr.; Oie, S.  
 CS University of California at San Francisco, CA, 94143-0446, USA  
 SO Proceedings of the International Symposium on Controlled Release of  
 Bioactive Materials (1997), 24th, 7-8  
 CODEN: PCRMEY; ISSN: 1022-0178  
 PB Controlled Release Society, Inc.  
 DT Journal  
 LA English  
 CC 63-5 (Pharmaceuticals)  
 Section cross-reference(s): 1  
 AB The intestinal absorption of peptides was increased by coupling to the 24  
 position of the steroid nucleus in cholic acid.  
 ST bile acid peptide delivery intestine  
 IT Drug delivery systems  
 Intestine

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(oral peptide delivery using intestinal bile acid transporter)

IT Bile acids  
Peptides, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oral peptide delivery using intestinal bile acid transporter)

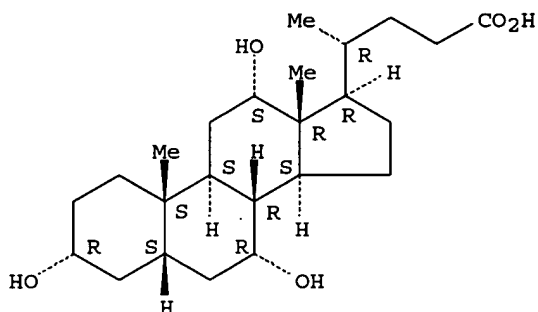
IT 81-25-4D, Cholic acid, peptide conjugates  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oral peptide delivery using intestinal bile acid transporter)

IT 81-25-4D, Cholic acid, peptide conjugates  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oral peptide delivery using intestinal bile acid transporter)

RN 81-25-4 HCAPLUS

CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ .alph  
a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 1997:443336 HCAPLUS  
DN 127:55909  
ED Entered STN: 17 Jul 1997  
TI Sulfate conjugates of ursodeoxycholic acid, and their beneficial  
use in inflammatory disorders and other applications  
IN Setchell, Kenneth D. R.  
PA Children's Hospital Medical Center, Philadelphia, USA  
SO PCT Int. Appl., 68 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM A61K031-575  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9718816	A2	19970529	WO 1996-US18487	19961119 <--
	WO 9718816	A3	19970626		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5763435	A	19980609	US 1995-560992	19951121 <--
	CA 2238040	AA	19970529	CA 1996-2238040	19961119 <--
	CA 2238040	C	20040713		
	AU 9677377	A1	19970611	AU 1996-77377	19961119 <--
	AU 709594	B2	19990902		
	EP 871452	A2	19981021	EP 1996-940516	19961119 <--

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI

CN 1211185	A	19990317	CN 1996-199708	19961119 <--
JP 2000500764	T2	20000125	JP 1997-519828	19961119 <--
BR 9611606	A	20001024	BR 1996-11606	19961119 <--
PL 186393	B1	20040130	PL 1996-326931	19961119 <--
US 6251884	B1	20010626	US 1998-28036	19980224 <--
NO 9802281	A	19980708	NO 1998-2281	19980519 <--
PRAI US 1995-560992	A	19951121	<--	
WO 1996-US18487	W	19961119	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 9718816	ICM	A61K031-575	
WO 9718816	ECLA	A61K031/575	<--
US 5763435	NCL	514/182.000	
	ECLA	A61K031/575	<--
US 6251884	NCL	514/182.000; 514/169.000	
	ECLA	A61K031/575	<--
AB	Pharmaceutically acceptable compns. including a sulfate of ursodeoxycholic acid (I), glyoursodeoxycholic acid, or tauroursodeoxycholic acid and a pharmacol. acceptable carrier are useful for treatment of mammals for disorders including inflammation of the gastrointestinal tract, colon cancer, rectum cancer, ulcerative colitis, adenomatous polyps, familial polyposis, hepatitis, etc. These compns. may be used to improve liver function or serum biochem. in liver disease, to increase bile flow, or to decrease biliary secretion of phospholipid or cholesterol. An isolated organ may be maintained in vitro by perfusion with a I sulfate. Thus, I was condensed with tert-butyldimethylsilyl chloride to form the 3-tert-butyldimethylsilyl ether, then with Ac2O to form I 3-tert-butyldimethylsilyl ether 7-acetate, hydrolyzed with HCl to I 7-acetate, condensed with ClSO3H to form I 7-acetate 3-sulfate, converted to the di-Na salt, and saponified with methanolic NaOH to I 3-sulfate.		
ST	ursodeoxycholate sulfate inflammation inhibitor; colon cancer ursodeoxycholate sulfate; rectum cancer ursodeoxycholate sulfate; liver disease ursodeoxycholate sulfate		
IT	Intestine, neoplasm (colon, inhibitors; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)		
IT	Antitumor agents (colon; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)		
IT	Digestive tract (disease, inflammation; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)		
IT	Anti-inflammatory agents (gastrointestinal; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)		
IT	Solutions (isotonic solns., for organ perfusion; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)		
IT	Intestine (large, disease, inflammation; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)		
IT	Bile acids RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (metabolism of; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)		
IT	Intestine Kidney Lung Organ preservation (perfusion fluid for; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)		
IT	Intestine, neoplasm		

(polyp, adenomatous; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine, neoplasm  
Intestine, neoplasm  
(rectum, inhibitors; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Antitumor agents  
Antitumor agents  
(rectum; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Phospholipids, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(secretion of, in bile; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine, disease  
Intestine, disease  
(small, inflammation; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Cholagogues  
Hepatitis  
Liver, disease  
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine, disease  
(ulcerative colitis; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Biological transport  
(uptake, of ursodeoxycholic acid by intestine, inhibition of; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 434-13-9, Lithocholic acid  
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
(formation from ursodeoxycholate; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 128-13-2, Ursodeoxycholic acid  
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)  
(intestinal absorption of; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 57-88-5, Cholesterol, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(secretion of, in bile; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 71781-68-5P 191286-16-5P 191286-18-7P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 68780-73-4, Ursodeoxycholic acid 3-sulfate 74723-13-0, Tauroursodeoxycholic acid 3-sulfate 74723-14-1 74723-15-2 74723-16-3 88426-32-8 109333-29-1 133429-88-6, Glycoursodeoxycholic acid 3-sulfate 191286-12-1  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 474-25-9, Chenodeoxycholic acid 2393-58-0,  $\alpha$ -Muricholic acid 2393-59-1,  $\beta$ -Muricholic acid 6830-03-1,  $\omega$ -Muricholic acid 114183-56-1 114183-57-2 163750-00-3

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
 (sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 18162-48-6, tert-Butyldimethylsilyl chloride  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

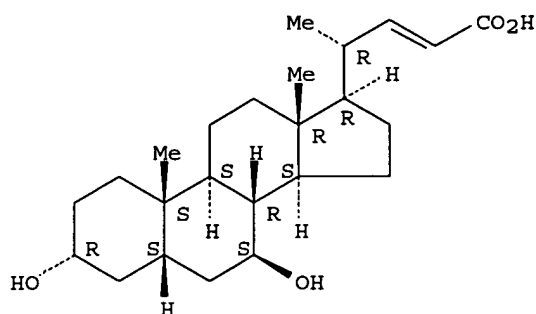
IT 71781-57-2P 71781-58-3P 75672-25-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 163750-00-3  
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
 (sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

RN 163750-00-3 HCAPLUS

CN Chol-22-en-24-oic acid, 3,7-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



L40 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1997:372273 HCAPLUS  
 DN 126:347323  
 ED Entered STN: 14 Jun 1997  
 TI Buccal delivery of glucagon-like insulinotropic peptides (GLPs)  
 IN Heiber, Sonia J.; Ebert, Charles D.; Gutniak, Mark K.  
 PA Theratech, Inc., USA  
 SO PCT Int. Appl., 55 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K009-70  
 ICS A61L015-16  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715296	A1	19970501	WO 1996-US16890	19961022 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
US 5766620	A	19980616	US 1995-553807	19951023 <--

Search done by Noble Jarrell

CA 2235369	AA	19970501	CA 1996-2235369	19961022 <--
AU 9674647	A1	19970515	AU 1996-74647	19961022 <--
AU 716038	B2	20000217		
EP 859606	A1	19980826	EP 1996-936815	19961022 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1202820	A	19981223	CN 1996-198618	19961022 <--
BR 9611139	A	19990406	BR 1996-11139	19961022 <--
JP 11513982	T2	19991130	JP 1996-516712	19961022 <--
TW 416854	B	20010101	TW 1996-85112962	19961022 <--
ZA 9608909	A	19970528	ZA 1996-8909	19961023 <--
US 5863555	A	19990126	US 1997-964731	19971105 <--
PRAI US 1995-553807	A	19951023	<--	
WO 1996-US16890	W	19961022	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 9715296	ICM	A61K009-70	
	ICS	A61L015-16	
US 5766620	NCL	424/436.000; 424/435.000; 514/772.300; 514/772.600; 514/774.000; 514/777.000; 514/781.000	
	ECLA	A61K009/00M18D; A61K038/26	<--
US 5863555	NCL	424/435.000; 514/772.300; 514/772.600; 514/774.000; 514/777.000; 514/781.000	
	ECLA	A61K038/26	<--

AB Drug delivery systems for administering a GLP to the buccal mucosa for transmucosal drug delivery comprise a drug composition containing effective amts. of the GLP and a permeation enhancer, and means for maintaining the drug composition in a drug-transferring relation with the buccal mucosa. These systems can be in free form, such as creams, gels, and ointments, or can comprise a device of determined phys. form, such as tablets, patches, and troches. A preferred GLP is GLP-1(7-36) amide. Thus, a gingival bilayer tablet was prepared comprising an active layer and an adhesive layer. The adhesive layer was prepared by mixing polyethylene oxide 70, Carbopol 934P 20, and compressible xylitol/CM-cellulose filler 10 weight parts, granulating with EtOH, sieving, drying, mixing with stearic acid 0.25 and mint flavor 0.06 weight%, and compression. To prepare the active layer, mannitol 49.39, hydroxypropylcellulose 34.33, and Na taurocholate 15.00 weight% were mixed, granulated with EtOH, sieved, dried, combined with GLP-1(7-36) amide 0.91, FD&C Yellow Number 6HT 0.06, Mg stearate 0.25, and mint flavor 0.06 weight%; 50 mg of this mixture was compressed onto 50 mg adhesive layer.

ST glucagonlike insulintropic peptide buccal tablet; mouth absorption  
glucagonlike insulintropic peptide

IT Alcohols, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(C2-3, permeation enhancers; buccal delivery of glucagon-like insulintropic peptides)

IT Glycols, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(C3-4; buccal delivery of glucagon-like insulintropic peptides)

IT Polyoxyalkylenes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(adhesive containing; buccal delivery of glucagon-like insulintropic peptides)

IT Caseins, biological studies  
Gelatins, biological studies  
Polyethers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(adhesives containing; buccal delivery of glucagon-like insulintropic peptides)

IT Adhesives  
(biol.; buccal delivery of glucagon-like insulintropic peptides)

IT Antidiabetic agents  
Gingiva  
Permeation enhancers  
(buccal delivery of glucagon-like insulintropic peptides)

- IT Sulfonylureas  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(buccal delivery of glucagon-like insulintropic peptides)
- IT Drug delivery systems  
(buccal; buccal delivery of glucagon-like insulintropic peptides)
- IT Steroids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(detergents, as permeation enhancers; buccal delivery of glucagon-like insulintropic peptides)
- IT Cell membrane  
(disrupting agents for; buccal delivery of glucagon-like insulintropic peptides)
- IT Drug delivery systems  
(gels; buccal delivery of glucagon-like insulintropic peptides)
- IT Polymers, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hydrophilic, adhesive containing; buccal delivery of glucagon-like insulintropic peptides)
- IT Drug delivery systems  
(lozenges; buccal delivery of glucagon-like insulintropic peptides)
- IT Mouth  
(mucosa; buccal delivery of glucagon-like insulintropic peptides)
- IT Drug delivery systems  
(ointments, creams; buccal delivery of glucagon-like insulintropic peptides)
- IT Drug delivery systems  
(ointments; buccal delivery of glucagon-like insulintropic peptides)
- IT Chelating agents  
Solvents  
Surfactants  
(permeation enhancers; buccal delivery of glucagon-like insulintropic peptides)
- IT Bile salts  
Fatty acids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(permeation enhancers; buccal delivery of glucagon-like insulintropic peptides)
- IT Vinyl compounds, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polymers, adhesives containing; buccal delivery of glucagon-like insulintropic peptides)
- IT Detergents  
(steroidal, as permeation enhancers; buccal delivery of glucagon-like insulintropic peptides)
- IT Drug delivery systems  
Drug delivery systems  
(tablets, buccal; buccal delivery of glucagon-like insulintropic peptides)
- IT 79-10-7D, 2-Propenoic acid, esters, polymers, biological studies  
79-10-7D, 2-Propenoic acid, polymers, biological studies 557-75-5D,  
Ethenol, polymers, biological studies 9000-30-0, Guar gum 9000-69-5,  
Pectin 9003-39-8, PVP 9004-32-4 9004-54-0, Dextran, biological  
studies 9004-57-3, Ethylcellulose 9004-62-0, Hydroxyethylcellulose  
9004-64-2, Hydroxypropylcellulose 9004-65-3,  
Hydroxypropylmethylcellulose 9005-25-8, Starch, biological studies  
25322-68-3  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(adhesive containing; buccal delivery of glucagon-like insulintropic peptides)
- IT 107444-51-9 118549-37-4, Insulintropin  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(buccal delivery of glucagon-like insulintropic peptides)

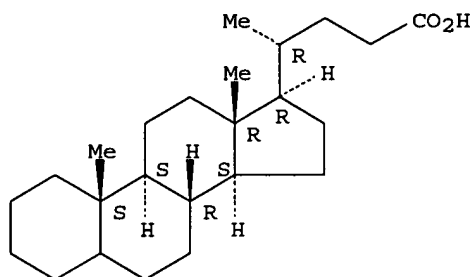
IT 67-68-5, biological studies 68-12-2, biological studies 102-76-1, Triacetin 108-32-7, Propylene carbonate 110-27-0, Isopropyl myristate 111-82-0, Methyl laurate 112-80-1, Oleic acid, biological studies 122-32-7, Glycerol trioleate 127-19-5 143-28-2, Oleyl alcohol 145-42-6, Sodium taurocholate 151-21-3, SDS, biological studies 872-50-4, N-Methylpyrrolidone, biological studies 3445-11-2, N-(2-Hydroxyethyl)-2-pyrrolidinone 5306-85-4, Dimethyl isosorbide 25496-72-4, Glycerol monooleate 25637-84-7, Glycerol dioleate 27194-74-7, Propylene glycol monolaurate 27215-38-9, Glycerol monolaurate 31566-31-1, Glycerol monostearate 59227-89-3  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (permeation enhancer; buccal delivery of glucagon-like insulinotropic peptides)

IT 107-35-7D, Taurine, bile acid conjugates, salts 12441-09-7D, Sorbitan, esters 25312-65-6D, Cholanic acid, salts  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

IT 25312-65-6D, Cholanic acid, salts  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

RN 25312-65-6 HCAPLUS  
 CN Cholan-24-oic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1997:218959 HCAPLUS  
 DN 126:308684  
 ED Entered STN: 04 Apr 1997  
 TI Use of the intestinal bile acid transporter for the uptake of cholic acid conjugates with HIV-1 protease inhibitory activity  
 AU Kagedahle, Matts; Swaan, Peter W.; Redemann, Carl T.; Tang, Mary; Craik, Charles S.; Szoka, Francis C., Jr.; Oie, Svein  
 CS Dep. Pharmacy Pharmaceutical Chem., Univ. California, San Francisco, CA, 94143-0446, USA  
 SO Pharmaceutical Research (1997), 14(2), 176-180  
 CODEN: PHREEB; ISSN: 0724-8741  
 PB Plenum  
 DT Journal  
 LA English  
 CC 63-5 (Pharmaceuticals)  
 Section cross-reference(s): 1

AB The purpose of this study was to investigate the ability of the human intestinal bile acid transporter to transport cholic acid conjugates with potential HIV-1 protease inhibitory activity. Cholic acid was conjugated at the 24 position of the sterol nucleus with various amino acids and amino acid analogs. The CaCo-2 cell line was used as a model to investigate the interaction of these bile acid conjugates with the human intestinal bile acid transporter. Interaction between the carrier and the conjugates was

quantified by inhibition of taurocholic acid transport and confirmed by transport of radiolabeled conjugates in this cell line. The highest interaction with the transporter, as quantified by inhibition of taurocholic acid transport, occurred when a single neg. charge was present around the 24 to 29 region of the sterol nucleus. A second neg. charge or a pos. charge significantly reduced the interaction. Transport of radiolabeled cholyl-L-Lys- $\epsilon$ -tBOC ester and cholyl-D-Asp- $\beta$ -benzyl ester was inhibited by taurocholic acid. Of all tested compds., only cholyl-D-Asp- $\beta$ -benzyl ester showed modest HIV-1 protease inhibitory activity with an IC<sub>50</sub> of 125  $\mu$ M. Cholic acid-amino acid conjugates with appropriate stereochem. are recognized and transported by the human bile acid transporter and show modest HIV-1 protease inhibitory activity. Transport of these conjugates by the bile acid carrier is influenced by charge and hydrophobicity around the 24 position of the sterol nucleus.

ST bile amino acid conjugate intestine transport; HIV1 protease inhibition cholate conjugate AIDS

IT Bile acids

RL: BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(conjugates, with amino acids; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Amino acids, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(conjugates, with bile acids; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Biological transport

(drug; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Drug delivery systems

(oral; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Bile acids

RL: BSU (Biological study, unclassified); BIOL (Biological study) (transporter; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Biological transport

(uptake; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Anti-AIDS agents

Hydrophobicity

Intestine

(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT 144114-21-6, Retropepsin

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(HIV-1; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT 7440-23-5, Sodium, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (bile acid transport dependent on; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT 2365-14-2P 28071-39-8P, Cholyl-L-lysine

73386-01-3P 89311-00-2P 106335-70-0P

189261-12-9P 189261-13-0P 189261-14-1P

189261-15-2P 189282-94-8P 189282-95-9P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological

process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT 81-25-4D, Cholic acid, conjugates with amino acids

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT 2365-14-2P 28071-39-8P, Cholyl-L-lysine

73386-01-3P 89311-00-2P 106335-70-0P

189261-12-9P 189261-13-0P 189261-14-1P

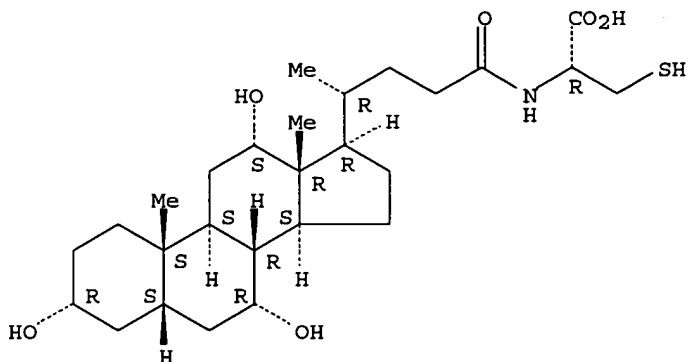
189261-15-2P 189282-94-8P 189282-95-9P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

RN 2365-14-2 HCAPLUS

CN L-Cysteine, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

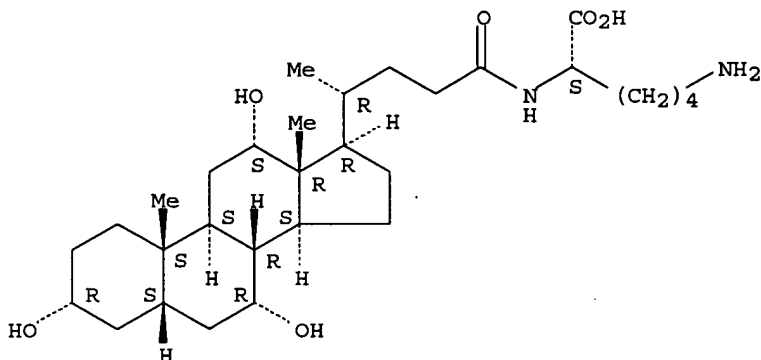
Absolute stereochemistry.



RN 28071-39-8 HCAPLUS

CN L-Lysine, N2-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

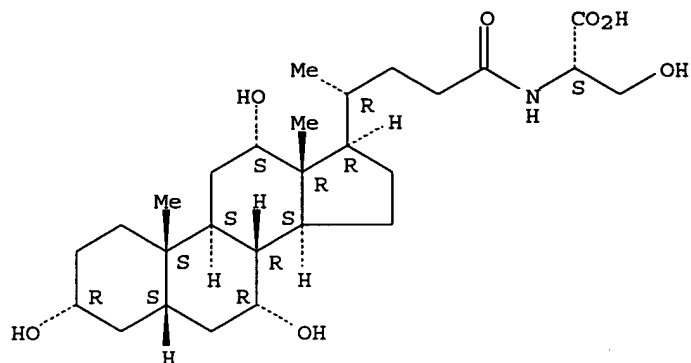
Absolute stereochemistry.



RN 73386-01-3 HCAPLUS

CN L-Serine, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

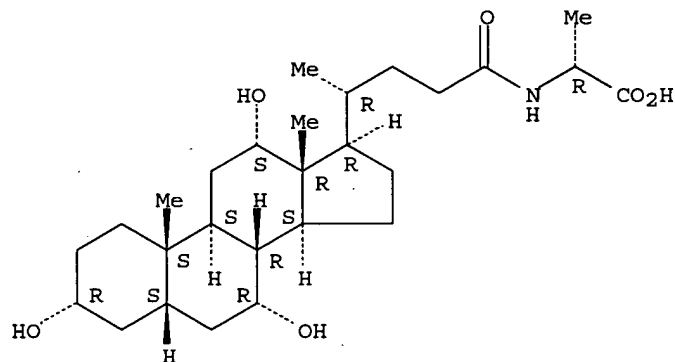
Absolute stereochemistry.



RN 89311-00-2 HCAPLUS

CN D-Alanine, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

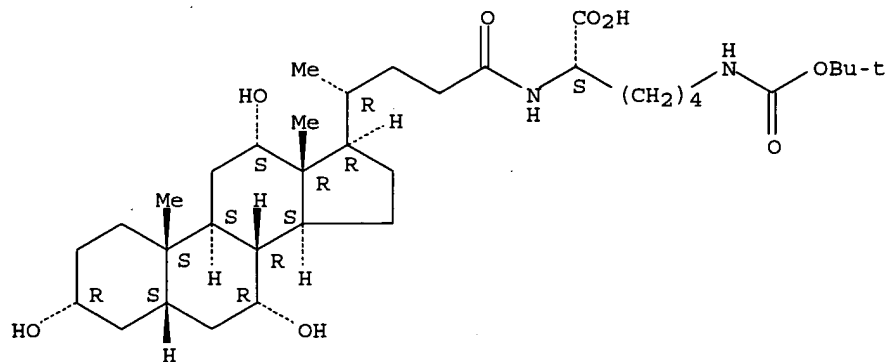
Absolute stereochemistry.



RN 106335-70-0 HCAPLUS

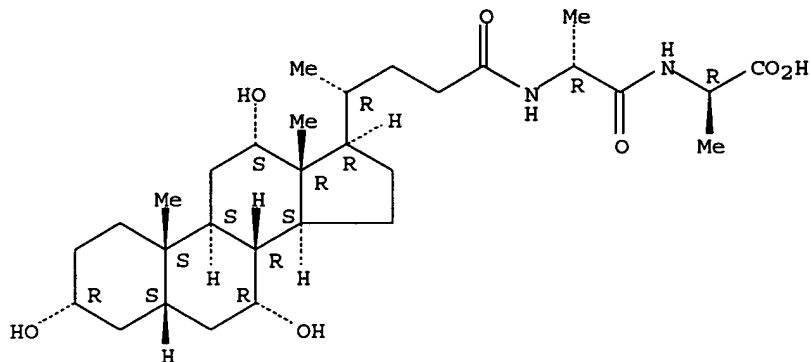
CN L-Lysine, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



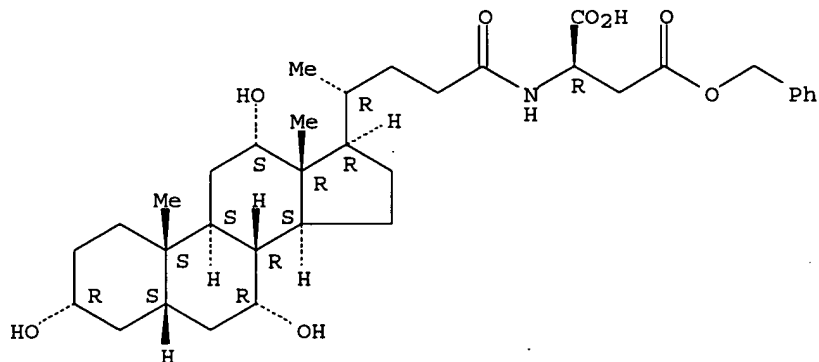
RN 189261-12-9 HCAPLUS  
 CN D-Alanine, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



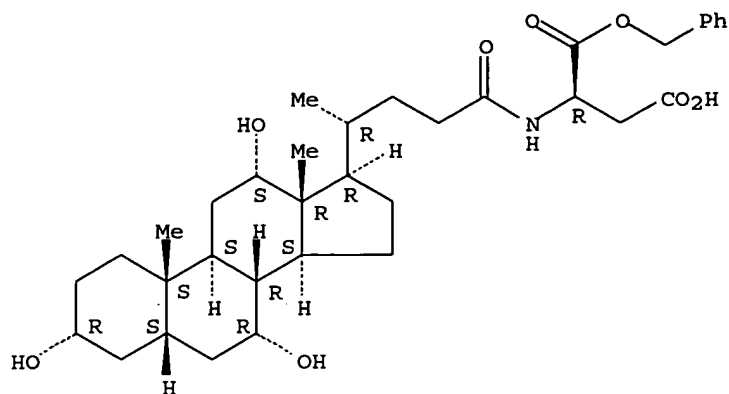
RN 189261-13-0 HCAPLUS  
 CN D-Aspartic acid, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-, 4-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 189261-14-1 HCAPLUS  
 CN D-Aspartic acid, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-, 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)

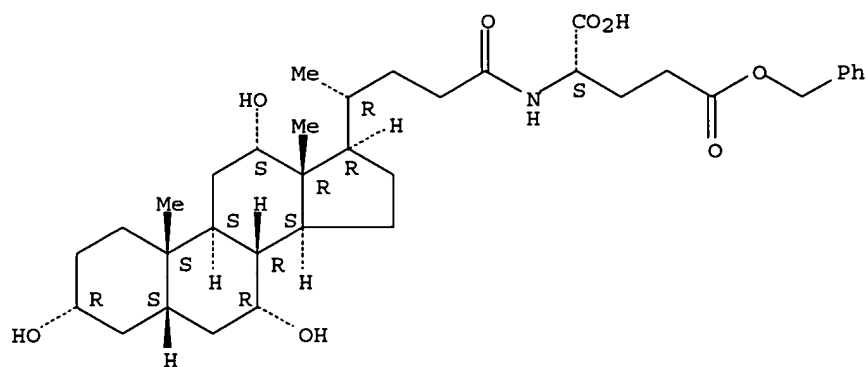
Absolute stereochemistry.



RN 189261-15-2 HCAPLUS

CN L-Glutamic acid, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-, 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

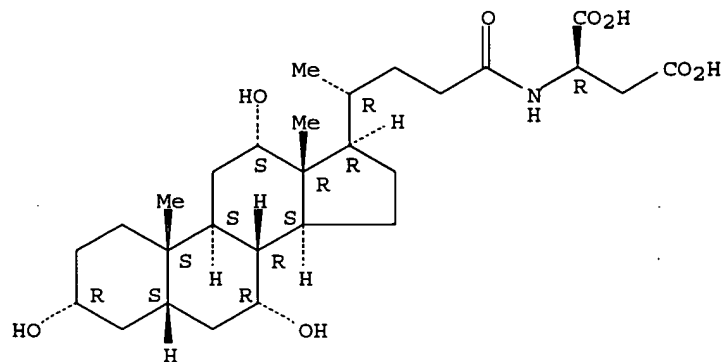
Absolute stereochemistry.



RN 189282-94-8 HCAPLUS

CN D-Aspartic acid, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

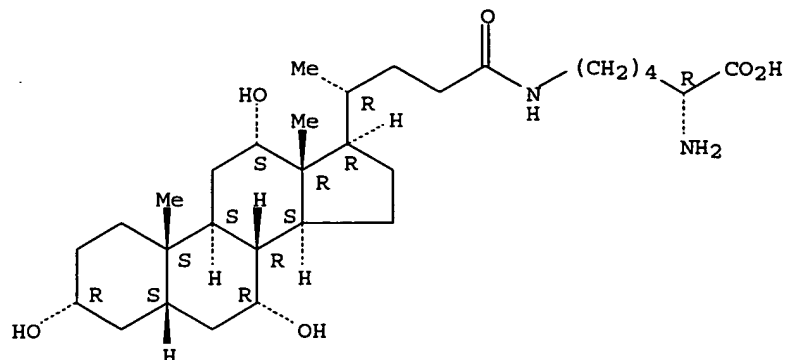
Absolute stereochemistry.



RN 189282-95-9 HCAPLUS

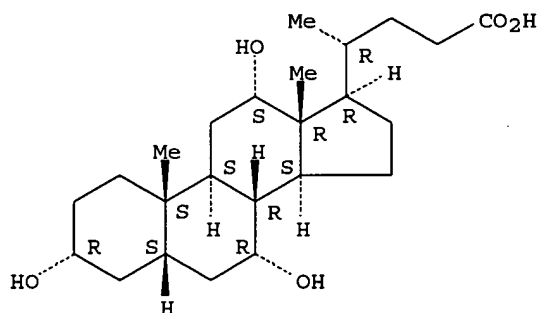
CN D-Lysine, N6-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 81-25-4D, Cholic acid, conjugates with amino acids  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)  
 RN 81-25-4 HCAPLUS  
 CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ .alph a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1995:721131 HCAPLUS  
 DN 123:322102  
 ED Entered STN: 05 Aug 1995  
 TI Acylated derivatives of human insulin with improved solubility and stability for treatment of diabetes  
 IN Havelund, Svend; Halstroem, John Broberg; Jonassen, Ib; Andersen, Asser Sloth; Markussen, Jan  
 PA Novo Nordisk A/S, Den.  
 SO PCT Int. Appl., 99 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07K014-62  
 ICS A61K038-28  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 2, 3  
 FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Search done by Noble Jarrell

PI WO 9507931 A1 19950323 WO 1994-DK347 19940916 <--  
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ZA 9407187 A 19950317 ZA 1994-7187 19940916 <--  
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WO 1994-DK347 W 19940916 <--

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9507931	ICM	C07K014-62
	ICS	A61K038-28
WO 9507931	ECLA	C07K014/62 <--
EP 1132404	ECLA	C07K014/62 <--

AB Novel human insulin derivs. with improved solubility and a protracted profile of action are described for use in the treatment of diabetes. These analogs have amino acid substitutions at amino acids A21 and B3 (any amino acid except Lys, Arg, or Cys); PheB1 may be deleted and B30 is substituted by a C10-24 lipophilic amino acid or any naturally occurring amino acid except Lys, Arg, or Cys; if B30 is a lipophilic amino acid, then the ε-NH2 group of LysB29 is acylated with a C≤5 carboxylic acid. They may be used in the treatment of diabetes in several pharmaceutical compns. presented. Chemical preparation of some of these analogs and the manufacture of the amino acid-substituted A and B chains by expression of the cloned cDNAs is demonstrated.

ST human insulin sequence acylation diabetes pharmaceutical

IT Protein sequences

- (acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Solubility  
(at physiol. pH; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Acetyl group  
Formyl group  
(insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Fatty acids, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Carboxylic acids, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Diabetes mellitus  
(insulin pharmaceutical composition for treatment of; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Plasmid and Episome  
(pAK-series and pKFN1627 and pEA-series; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Carboxylic acids, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(C5, insulins modified with; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Deoxyribonucleic acid sequences  
(complementary, acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Carboxylic acids, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(di-, C<6, insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Pharmaceutical dosage forms  
(injections, insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT Functional groups  
(propionyl, insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT 11061-68-ODP, Insulin (human), amino acid-substituted and lipophilic amino acid-containing derivs.  
RL: BPN (Biosynthetic preparation); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT 9002-07-7D, Trypsin, immobilized 123175-82-6D, Proteinase, lysine-specific, immobilized  
RL: CAT (Catalyst use); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)  
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT 14464-31-4, Palmitic acid N-hydroxysuccinimide ester 69888-86-4  
88404-23-3 104943-24-0 165893-02-7 165893-03-8 168986-19-4  
168986-20-7 169142-69-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT 168986-17-2P 168986-18-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
- IT 23713-49-7DP, Zn<sup>2+</sup>, complexes with insulin derivs., preparation

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (acylated derivs. of human insulin with improved solubility and stability  
 for treatment of diabetes)

IT 169535-16-4P 169535-18-6P 169535-20-0P 169535-22-2P 169535-28-8P  
 169535-30-2P 169535-32-4P 169535-34-6P 169535-36-8P 169535-38-0P  
 RL: BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or  
 recovery); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (amino acid sequence; acylated derivs. of human insulin with improved  
 solubility and stability for treatment of diabetes)

IT 120177-51-7P 169148-61-2P 169148-75-8P  
 RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN  
 (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (amino acid sequence; acylated derivs. of human insulin with improved  
 solubility and stability for treatment of diabetes)

IT 39416-73-4P 169148-55-4DP, zinc complexes 169148-56-5DP, zinc  
 complexes 169148-57-6P 169148-58-7P 169148-59-8P 169148-60-1P  
 169148-62-3DP, zinc complexes 169148-63-4P 169148-64-5P 169148-65-6P  
 169148-66-7P 169148-67-8P 169148-68-9P 169148-69-0P 169148-70-3P  
 169148-71-4P 169148-72-5DP, zinc complexes 169148-72-5P 169148-73-6P  
 169148-74-7P  
 RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic  
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (amino acid sequence; acylated derivs. of human insulin with improved  
 solubility and stability for treatment of diabetes)

IT 141537-81-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (conjugation to insulin; acylated derivs. of human insulin  
 with improved solubility and stability for treatment of diabetes)

IT 168986-14-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (for conjugation to insulin; acylated derivs. of human  
 insulin with improved solubility and stability for treatment of diabetes)

IT 7452-59-7, n-Octyl chloroformate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (in preparation active ester derivs.; acylated derivs. of human insulin with  
 improved solubility and stability for treatment of diabetes)

IT 14565-47-0 22102-66-5 104211-94-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (in preparation chemical modified insulin analogs; acylated derivs. of human  
 insulin with improved solubility and stability for treatment of diabetes)

IT 108-30-5, Succinic anhydride, reactions 158627-30-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (in preparation myristic acid derivative for conjugation to insulin;  
 acylated derivs. of human insulin with improved solubility and stability for  
 treatment of diabetes)

IT 168986-15-0P 168986-16-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (in preparation myristic acid derivative for conjugation to insulin;  
 acylated derivs. of human insulin with improved solubility and stability for  
 treatment of diabetes)

IT 11075-17-5, Carboxypeptidase A  
 RL: CAT (Catalyst use); USES (Uses)  
 (in preparation of insulin derivs.; acylated derivs. of human insulin with  
 improved solubility and stability for treatment of diabetes)

IT 51-49-0, D-Thyroxine 68528-80-3, Disuccinimidyl suberate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (in preparation thyroxine derivative for conjugation to insulin;  
 acylated derivs. of human insulin with improved solubility and stability for  
 treatment of diabetes)

IT 110-15-6, Butanedioic acid, reactions 143-07-7, Dodecanoic acid,  
 reactions 638-53-9, Tridecanoic acid 7145-63-3, 2-Aminotetradecanoic

RL: RCT (Reactant); RACT (Reactant or reagent)

IT 544-63-8, Tetradecanoic acid, reactions

(insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

169535-25-5P      169535-26-6P      169535-27-7P      169535-29-9P      169535-31-3P

RL: BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

IT 24424-99-5, Di-tert-butyl pyrocarbonate

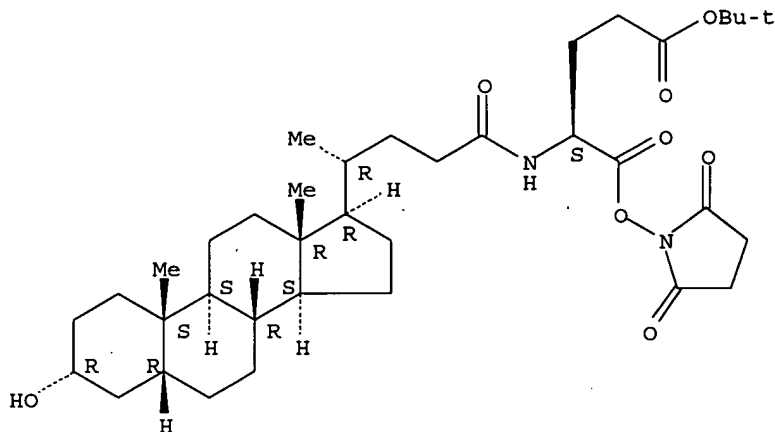
(protecting group, in preparation of insulin derivs.; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

RL: RCT (Reactant); RACT (Reactant or reagent)

(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-[[ (3 $\alpha$ ,5 $\beta$ )-3-hydroxy-24-oxocholan-24-yl]amino]-5-oxo-, 1,1-dimethylethyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

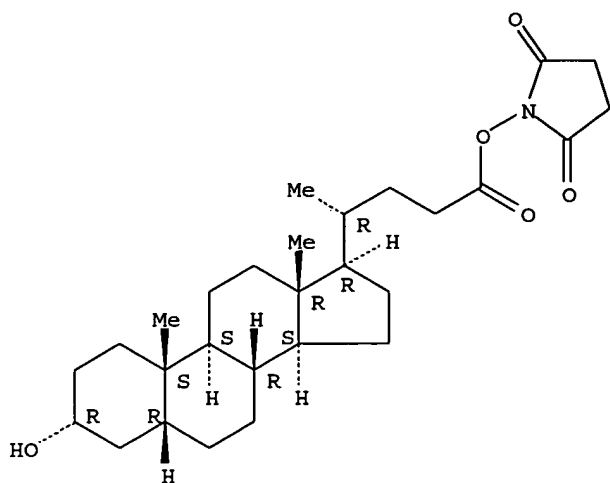


RL: RCT (Reactant); RACT (Reactant or reagent)

(in preparation chemical modified insulin analogs; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

CN 2,5-Pyrrolidinedione, 1-[[ (3 $\alpha$ ,5 $\beta$ )-3-hydroxy-24-oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:96130 HCAPLUS

DN 122:3980

ED Entered STN: 08 Nov 1994

TI Bile salts of the toad, *Bufo marinus*: characterization of a new unsaturated higher bile acid, 3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ , 26-tetrahydroxy-5 $\beta$ -cholest-23-en-27-oic acid

AU Yoshii, Michiko; Une, Mizuho; Kihira, Kenji; Kuramoto, Taiju; Akizawa, Toshifumi; Yoshioka, Masanori; Butler, Vincent P., Jr.; Hoshita, Takahiko

CS Sch. Med., Hiroshima Univ., Hiroshima, 734, Japan

SO Journal of Lipid Research (1994), 35(9), 1646-51

CODEN: JLPRAW; ISSN: 0022-2275

DT Journal

LA English

CC 6-5 (General Biochemistry)

AB The bile salts present in gallbladder bile of the toad, *Bufo marinus*, were found to consist of a mixture of bile alc. sulfates and unconjugated bile acids. The major bile alc. was 5 $\beta$ -bufol; 5 $\alpha$ - and 5 $\beta$ -cholestane-3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ , 26-tetrols occurred as the minor bile alcs. Bile acids of *Bufo marinus* were cholic acid, allocholic acid, 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-5 $\alpha$ - and 5 $\beta$ -cholestan-26-oic acids, 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-5 $\alpha$ - and 5 $\beta$ -cholest-23-en-26-oic acids, 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ ,26-tetrahydroxy-5 $\beta$ -cholestan-27-oic acid, and a C27 bile acid which has not been previously described. By chromatog. behavior, mass spectral data, and identification of the products of catalytic hydrogenation and ozonolysis, the structure of the new higher bile acid was elucidated as 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ ,26-tetrahydroxy-5 $\beta$ -cholest-23-en-27-oic acid. The bile salt pattern of *Bufo marinus* closely resembles that of *Bufo vulgaris formosus*, except for the absence of 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-5 $\beta$ -cholest-22-ene-24-carboxylic acid, the major bile acid of the later toad.

ST *Bufo* bile salt tetrahydroxycholestenoic acid

IT Bile

*Bufo marinus*

(bile acids and bile salts of *Bufo marinus*)

IT Bile acids

Bile salts

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);

BIOL (Biological study); OCCU (Occurrence)

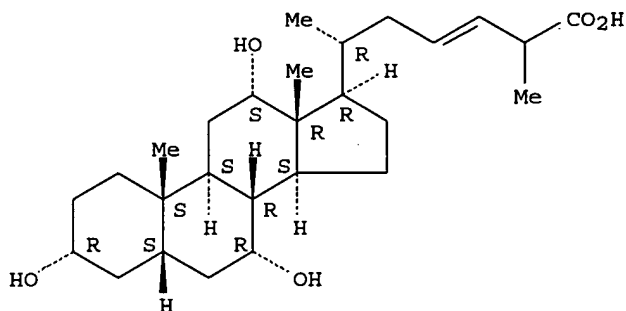
(bile acids and bile salts of *Bufo marinus*)

IT 81-25-4, Cholic acid 547-98-8 862-52-2D, 5 $\alpha$ -Cholestane-3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ , 26-tetrol, sulfate esters 862-53-3D,

5 $\beta$ -Cholestane-3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ , 26-tetrol, sulfate esters 2464-18-8 6127-75-9D, sulfate esters 17708-88-2,  
 3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ -Trihydroxy-5 $\alpha$ -cholestan-26-oic acid  
 73834-17-0 84888-63-1 88498-08-2 159330-16-2  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
 BIOL (Biological study); OCCU (Occurrence)  
 (bile acids and bile salts of *Bufo marinus*)

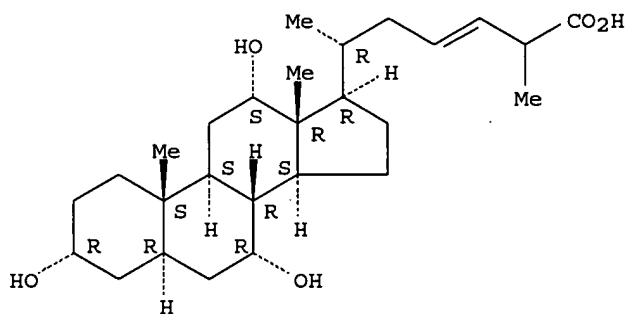
IT 84888-63-1 88498-08-2  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
 BIOL (Biological study); OCCU (Occurrence)  
 (bile acids and bile salts of *Bufo marinus*)  
 RN 84888-63-1 HCAPLUS  
 CN Cholest-23-en-26-oic acid, 3,7,12-trihydroxy-,  
 (3 $\alpha$ , 5 $\beta$ , 7 $\alpha$ , 12 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



RN 88498-08-2 HCAPLUS  
 CN Cholest-23-en-26-oic acid, 3,7,12-trihydroxy-,  
 (3 $\alpha$ , 5 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



L40 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1994:686635 HCAPLUS  
 DN 121:286635  
 ED Entered STN: 10 Dec 1994  
 TI Compositions containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease  
 IN Sipos, Tibor  
 PA Digestive Care Inc., USA  
 SO U.S., 9 pp.  
 CODEN: USXXAM  
 DT Patent

LA English  
 IC ICM A61K031-56  
 INCL 514182000  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1, 26

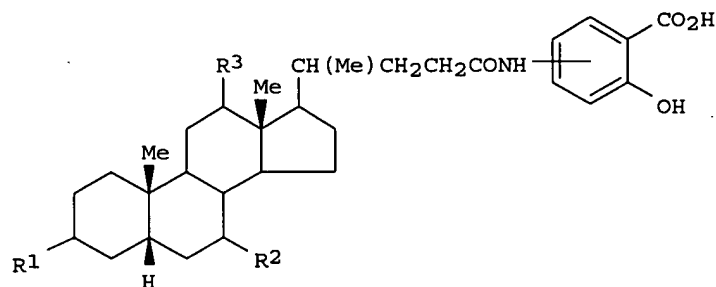
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5352682	A	19941004	US 1993-27693	19930308 <--
PRAI	US 1993-27693		19930308	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5352682	ICM	A61K031-56
	INCL	514182000
US 5352682	NCL	514/182.000; 424/451.000; 514/788.100; 552/553.000; 552/554.000
	ECLA	A61K031/60

OS MARPAT 121:286635  
 GI



AB Disclosed are compns. containing bile acid-aminosalicylate conjugates  
 I (R1 = OH in  $\alpha$  or  $\beta$  position; R2 = OH; R3 = H, OH; R4 = H, acetyl) or a pharmaceutically acceptable salt thereof. Also disclosed are a process for preparing the conjugates and methods for treating/preventing gastrointestinal disorders, impaired liver function, etc. using the conjugates.

ST bile acid aminosalicylate conjugate prepn therapeutic;  
 pharmaceutical bile acid aminosalicylate conjugate; deficiency disease bile acid aminosalicylate conjugate; antiinflammatory pharmaceutical bile acid aminosalicylate conjugate

IT Inflammation inhibitors  
 Pharmaceutical dosage forms  
 (compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Therapeutics  
 (for bile acid deficiency disease; compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Pharmaceutical dosage forms  
 (caplets, compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Bile acids  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (conjugates, with aminosalicylates; compns. containing acid-aminosalicylate conjugates or salts thereof for

treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Bile acids

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(metabolic disorders, deficiency, disease; compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Pharmaceutical dosage forms

(microspheres, compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Pharmaceutical dosage forms

(microtablets, compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT 28088-64-4DP, Aminosalicyclic acid, bile acid conjugates

159026-16-1P 159026-17-2P 159026-20-7P

159026-23-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT 159026-15-0 159026-18-3 159026-19-4

159026-21-8 159026-22-9 159026-24-1

159026-25-2 159026-26-3 159026-27-4

159026-28-5 159026-29-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT 37289-07-9, Cholyglycine hydrolase

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease in relation to conjugate hydrolysis)

IT 65-49-6, 4-Aminosalicyclic acid 81-25-4, Cholic acid 89-57-6,

5-Aminosalicyclic acid 128-13-2, Ursodeoxycholic acid

474-25-9, Chenodeoxycholic acid

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of and compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT 159026-16-1P 159026-17-2P 159026-20-7P

159026-23-0P

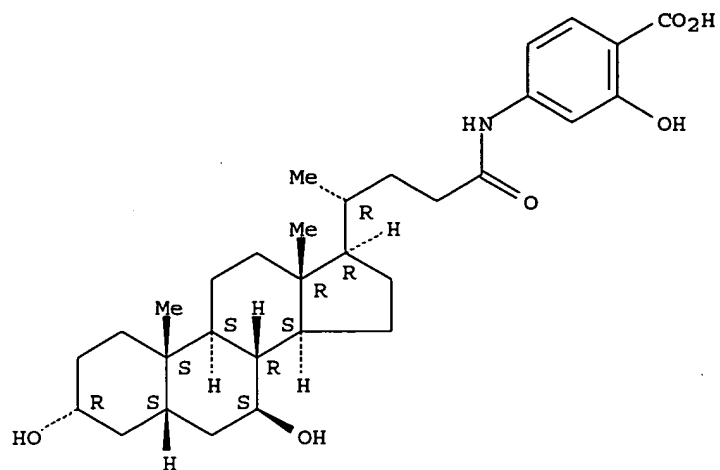
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

RN 159026-16-1 HCAPLUS

CN Benzoic acid, 4-[[ (3 $\alpha$ , 5 $\beta$ , 7 $\beta$ )-3, 7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

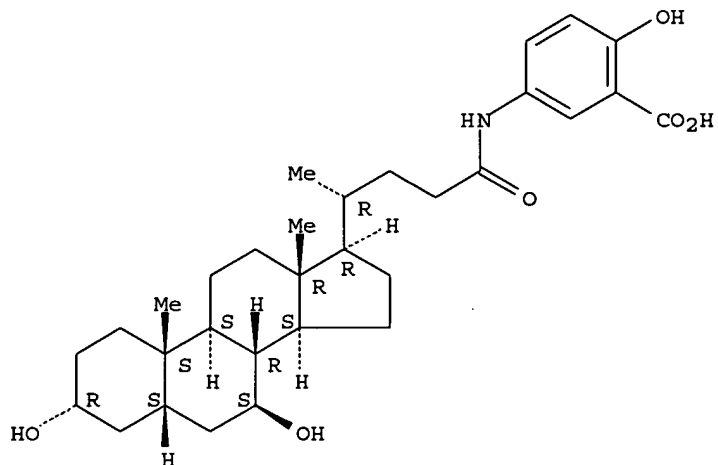
Absolute stereochemistry.



RN 159026-17-2 HCAPLUS

CN Benzoic acid, 5-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

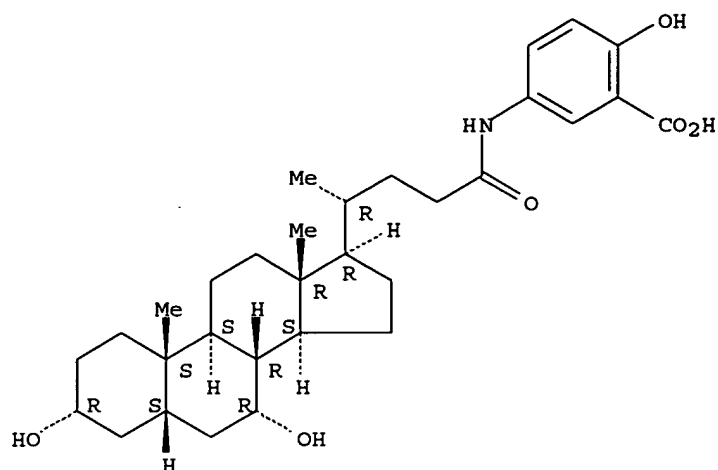
Absolute stereochemistry.



RN 159026-20-7 HCAPLUS

CN Benzoic acid, 5-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

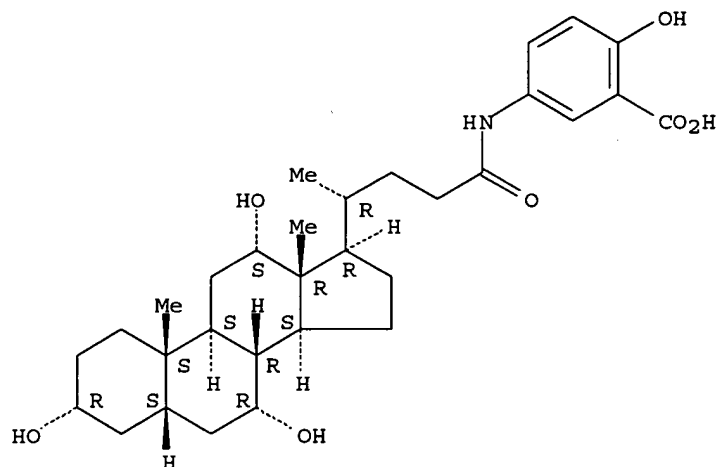
Absolute stereochemistry.



RN 159026-23-0 HCAPLUS

CN Benzoic acid, 2-hydroxy-5-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 159026-15-0 159026-18-3 159026-19-4

159026-21-8 159026-22-9 159026-24-1

159026-25-2 159026-26-3 159026-27-4

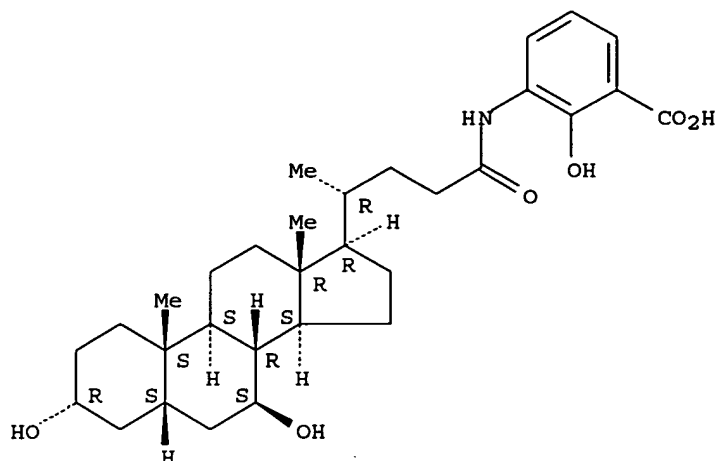
159026-28-5 159026-29-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(comps. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

RN 159026-15-0 HCAPLUS

CN Benzoic acid, 3-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

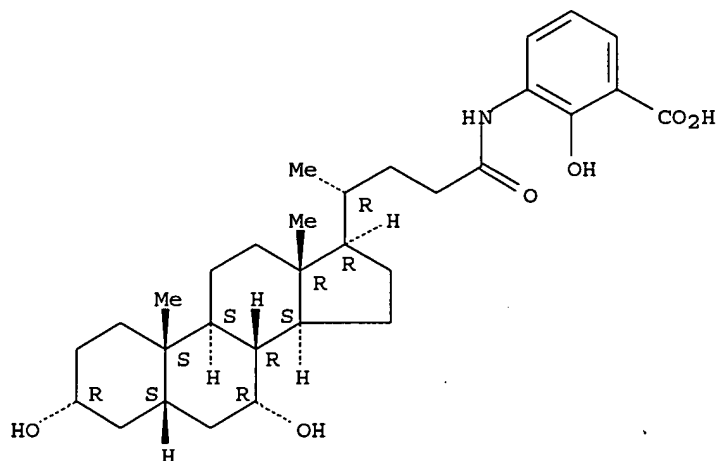
Absolute stereochemistry.



RN 159026-18-3 HCAPLUS

CN Benzoic acid, 3-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

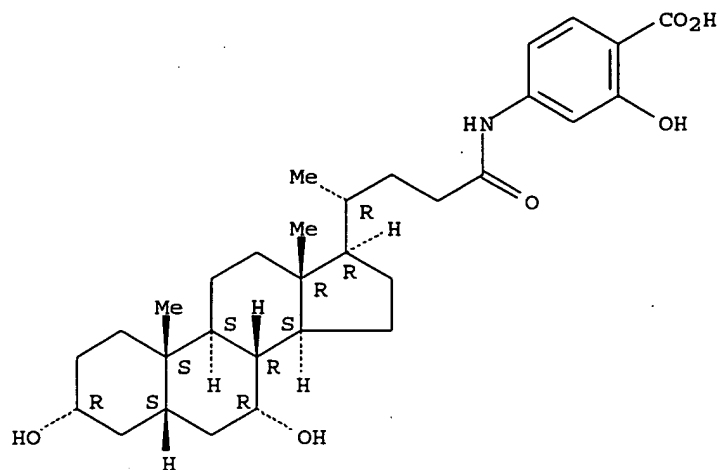
Absolute stereochemistry.



RN 159026-19-4 HCAPLUS

CN Benzoic acid, 4-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

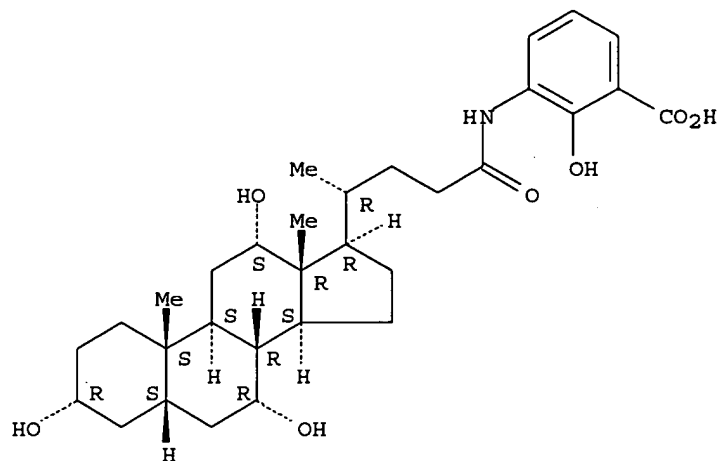
Absolute stereochemistry.



RN 159026-21-8 HCAPLUS

CN Benzoic acid, 2-hydroxy-3-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

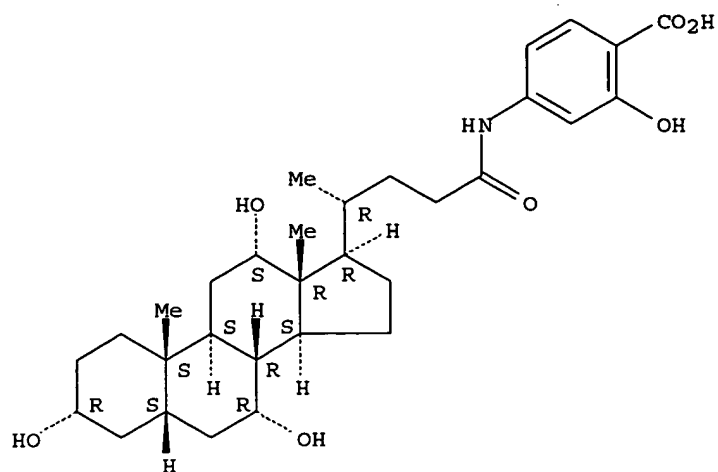
Absolute stereochemistry.



RN 159026-22-9 HCAPLUS

CN Benzoic acid, 2-hydroxy-4-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

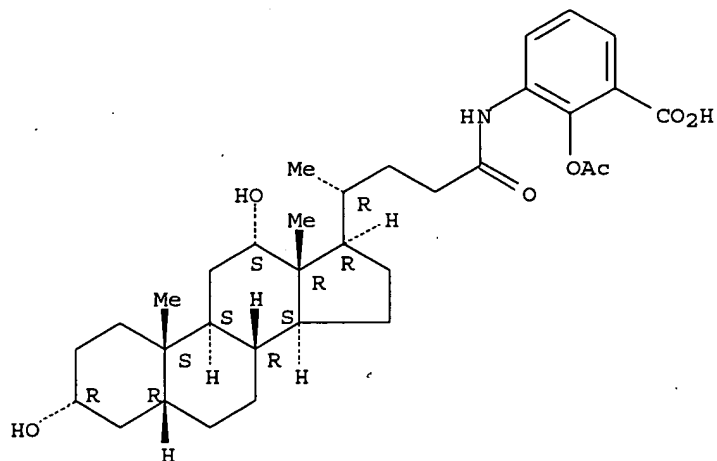
Absolute stereochemistry.



RN 159026-24-1 HCAPLUS

CN Benzoic acid, 2-(acetyloxy)-3-[[[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

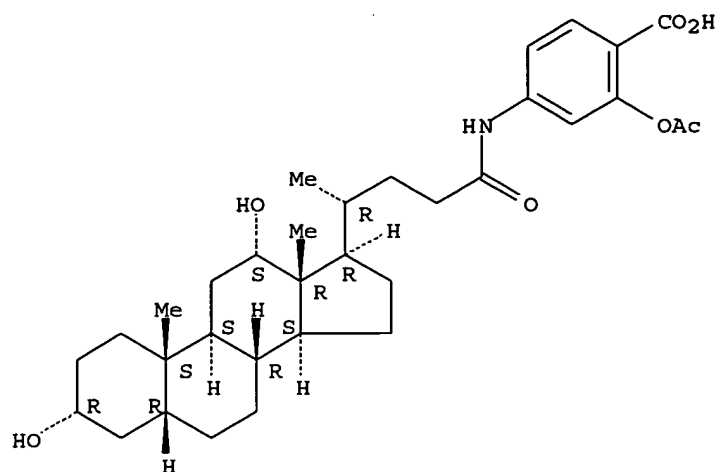
Absolute stereochemistry.



RN 159026-25-2 HCAPLUS

CN Benzoic acid, 2-(acetyloxy)-4-[[[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

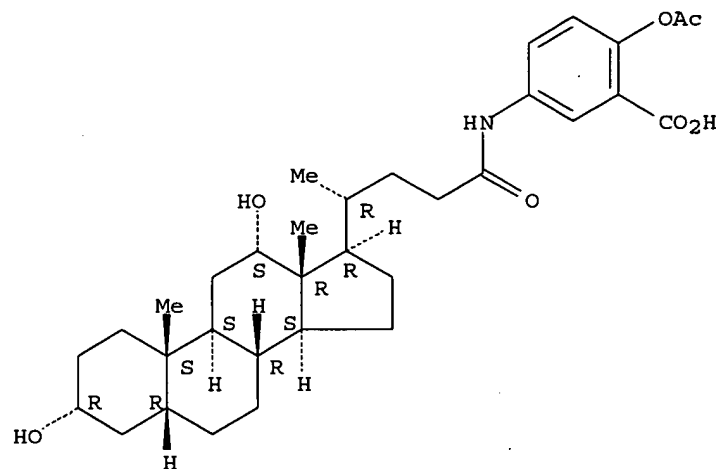
Absolute stereochemistry.



RN 159026-26-3 HCAPLUS

CN Benzoic acid, 2-(acetyloxy)-5-[[[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

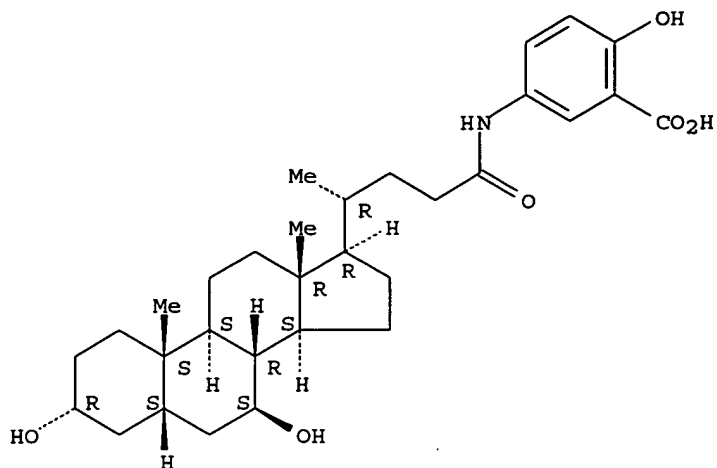


RN 159026-27-4 HCAPLUS

CN Benzoic acid, 5-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy-, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

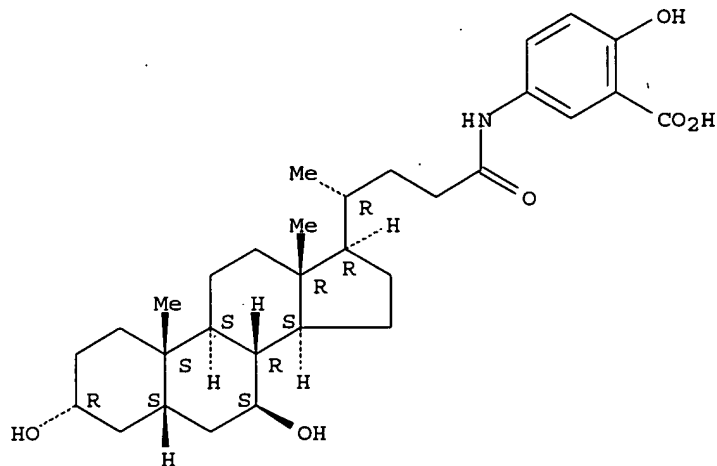
●x Na

RN 159026-28-5 HCAPLUS

CN Benzoic acid, 5-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy-, potassium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

●x K

RN 159026-29-6 HCAPLUS

CN Benzoic acid, 5-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy-, compd. with 2-amino-2-(hydroxymethyl)-1,3-

Search done by Noble Jarrell

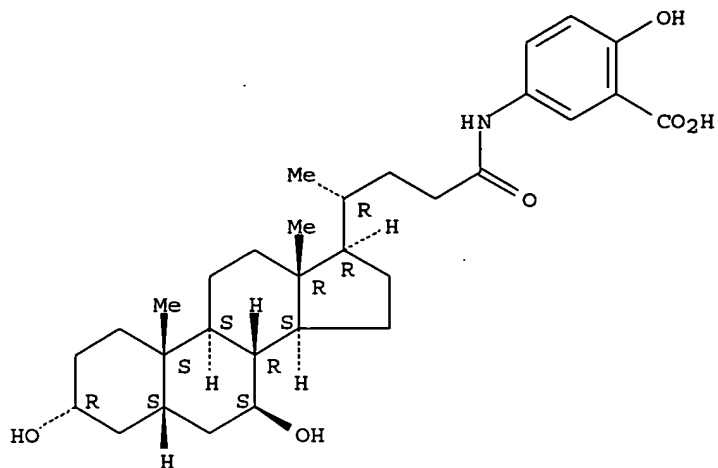
propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 159026-17-2

CMF C31 H45 N O6

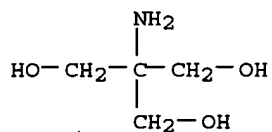
Absolute stereochemistry.



CM 2

CRN 77-86-1

CMF C4 H11 N O3



IT 81-25-4, Cholic acid 128-13-2, Ursodeoxycholic acid

474-25-9, Chenodeoxycholic acid

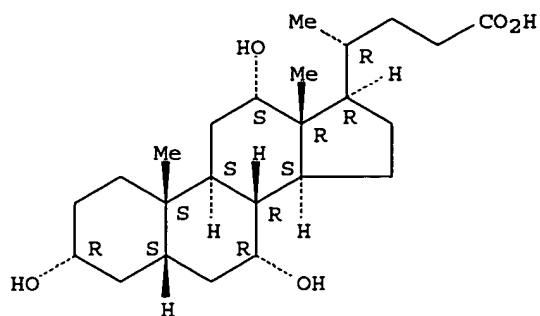
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of and compns. containing acid-aminosalicylate conjugates  
or salts thereof for treating/preventing a bile acid deficiency  
condition and inflammatory disease)

RN 81-25-4 HCAPLUS

CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ .alph  
a.)- (9CI) (CA INDEX NAME)

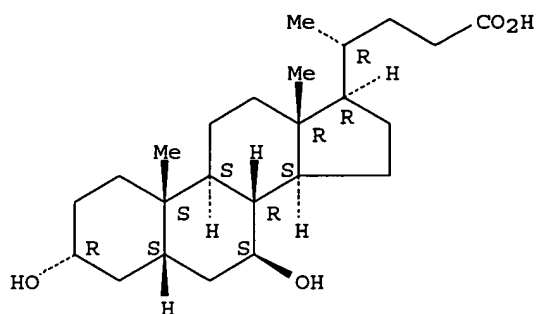
Absolute stereochemistry.



RN 128-13-2 HCAPLUS

CN Cholan-24-oic acid, 3,7-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )- (9CI) (CA INDEX NAME)

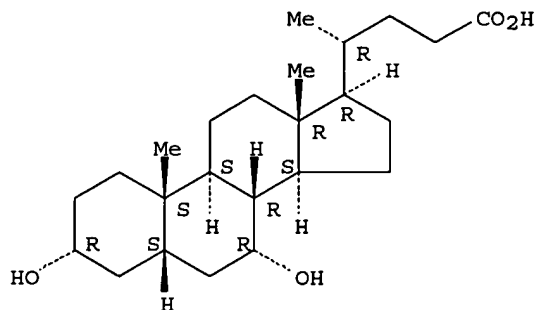
Absolute stereochemistry.



RN 474-25-9 HCAPLUS

CN Cholan-24-oic acid, 3,7-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1994:173477 HCAPLUS

DN 120:173477

ED Entered STN: 02 Apr 1994

TI The use of nor- and homo- bile acid derivatives as absorption enhancers for medicaments

IN Berlati, Fabio; Ceschel, Giancarlo; Roda, Aldo; Roda, Enrico; Ronchi, Celestino

PA Montereisearch S.r.l., Italy

SO PCT Int. Appl., 14 pp.

CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K047-28  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 1

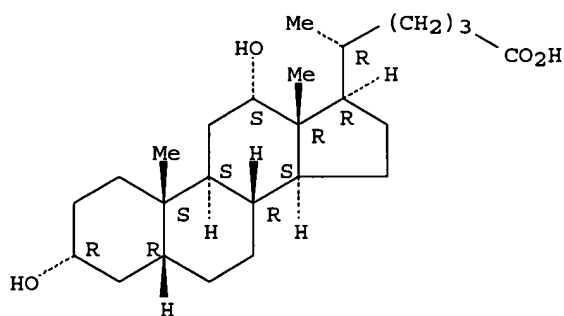
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9400155	A1	19940106	WO 1993-EP1508	19930615 <--
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 652773	A1	19950517	EP 1993-912975	19930615 <--
	EP 652773	B1	19980107		
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	JP 07508013	T2	19950907	JP 1993-501998	19930615 <--
	AT 161731	E	19980115	AT 1993-912975	19930615 <--
	ES 2114056	T3	19980516	ES 1993-912975	19930615 <--
	US 5656277	A	19970812	US 1994-360833	19941228 <--
PRAI	IT 1992-MI1601	A	19920630	<--	
	WO 1993-EP1508	W	19930615	<--	

## CLASS

	PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
	WO 9400155	ICM	A61K047-28
	US 5656277	NCL	424/400.000; 424/435.000; 424/436.000; 424/451.000; 424/464.000; 424/489.000; 514/169.000; 514/171.000; 514/182.000; 514/553.000; 514/569.000
		ECLA	A61K047/28 <--
AB	Nor- and homo- bile acid derivs. and their conjugates with taurine, glycine, and alanine in C23 and C25 are used as absorption enhancers for medicaments administered by the enteral route or by other routes, such as intranasal, buccal and sublingual routes. The derivs. improve the absorption of medicaments through mucosa without being metabolized by the intestinal flora, thus allowing a fast excretion. Moreover, the derivs. have a negligible toxicity. For example, a suppository contained Na diclofenac 0.1, homochenodeoxycholic acid 0.02, and Witepsol H-15 2.5g.		
ST	bile acid drug absorption enhancer; norbile acid drug absorption enhancer		
IT	Bile acids RL: BIOL (Biological study) (as absorption enhancers for drugs)		
IT	Antihistaminics Cardiovascular agents Cholinergic antagonists Diuretics Inflammation inhibitors Hormones Steroids, biological studies RL: BIOL (Biological study) (dosage forms of, bile acid derivs. as absorption enhancers in)		
IT	Peptides, biological studies RL: BIOL (Biological study) (drugs, dosage forms of, bile acid derivs. as absorption enhancers in)		
IT	Pharmaceutical dosage forms (buccal, bile acid derivs. as absorption enhancers in)		
IT	Bile acids RL: BIOL (Biological study) (conjugates, with taurine and glycine and alanine, as absorption enhancers for drugs)		
IT	Anesthetics (local, dosage forms of, bile acid derivs. as absorption enhancers in)		
IT	Pharmaceutical dosage forms (nasal, bile acid derivs. as absorption enhancers in)		
IT	Bile acids RL: BIOL (Biological study) (nor-, 3,7-dihydroxy, as absorption enhancers for drugs)		

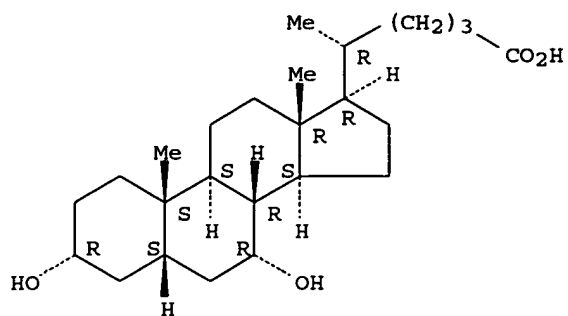
- IT Pharmaceutical dosage forms  
(suppositories, bile acid derivs. as absorption enhancers in)
- IT Pharmaceutical dosage forms  
(tablets, bile acid derivs. as absorption enhancers in)
- IT 38636-77-0 38636-78-1D, Homochenodeoxycholic acid,  
conjugates 53608-86-9, Nordeoxycholic acid  
86386-61-0, Norchenodeoxycholic acid 99697-24-2,  
Norursodeoxycholic acid 102044-28-0 153311-78-5  
153311-79-6 153311-80-9 153481-25-5  
RL: BIOL (Biological study)  
(as absorption enhancer for drugs)
- IT 56-40-6D, Glycine, conjugates with bile acids 56-41-7D,  
Alanine, conjugates with bile acids 107-35-7D, Taurine,  
conjugates with bile acids  
RL: BIOL (Biological study)  
(as absorption enhancers for drugs)
- IT 9034-40-6, LHRH  
RL: BIOL (Biological study)  
(buccal dosage forms containing, bile acid derivs. as absorption enhancers in)
- IT 9007-12-9, Calcitonin  
RL: BIOL (Biological study)  
(rectal capsules containing, bile acid derivs. as absorption enhancers in)
- IT 15307-79-6, Sodium diclofenac  
RL: BIOL (Biological study)  
(suppository containing, bile acid derivs. as absorption enhancers in)
- IT 54-31-9, Furosemide 68-89-3, Dipyrone 443-48-1, Metronidazole  
RL: BIOL (Biological study)  
(tablets containing, bile acid derivs. as absorption enhancers in)
- IT 38636-77-0 38636-78-1D, Homochenodeoxycholic acid,  
conjugates 53608-86-9, Nordeoxycholic acid  
86386-61-0, Norchenodeoxycholic acid 99697-24-2,  
Norursodeoxycholic acid 102044-28-0 153311-78-5  
153311-80-9  
RL: BIOL (Biological study)  
(as absorption enhancer for drugs)
- RN 38636-77-0 HCAPLUS
- CN Cholan-24-carboxylic acid, 3,12-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



- RN 38636-78-1 HCAPLUS
- CN Cholan-24-carboxylic acid, 3,7-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )-  
(9CI) (CA INDEX NAME)

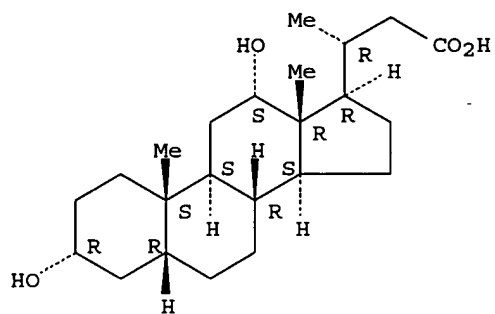
Absolute stereochemistry.



RN 53608-86-9 HCAPLUS

CN 24-Norcholan-23-oic acid, 3,12-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-  
(9CI) (CA INDEX NAME)

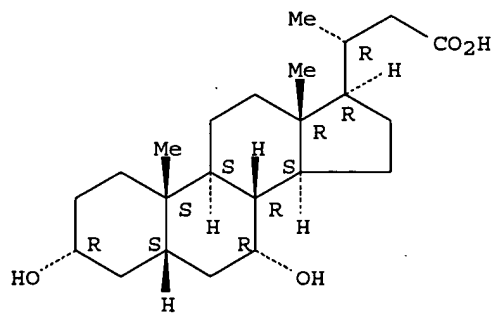
Absolute stereochemistry.



RN 86386-61-0 HCAPLUS

CN 24-Norcholan-23-oic acid, 3,7-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )-  
(9CI) (CA INDEX NAME)

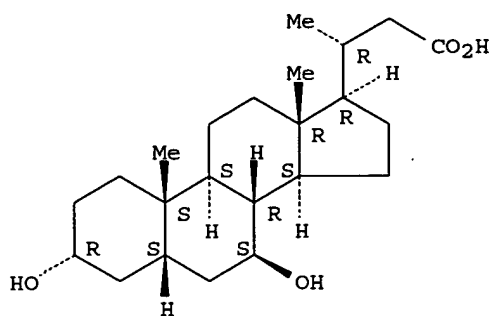
Absolute stereochemistry.



RN 99697-24-2 HCAPLUS

CN 24-Norcholan-23-oic acid, 3,7-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )-  
(9CI) (CA INDEX NAME)

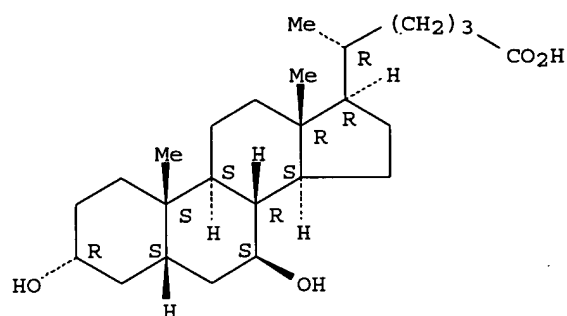
Absolute stereochemistry.



RN 102044-28-0 HCAPLUS

CN Cholan-24-carboxylic acid, 3,7-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )-  
(9CI) (CA INDEX NAME)

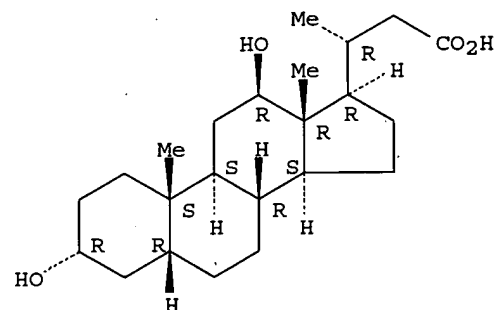
Absolute stereochemistry.



RN 153311-78-5 HCAPLUS

CN 24-Norcholan-23-oic acid, 3,12-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,12 $\beta$ )-  
(9CI) (CA INDEX NAME)

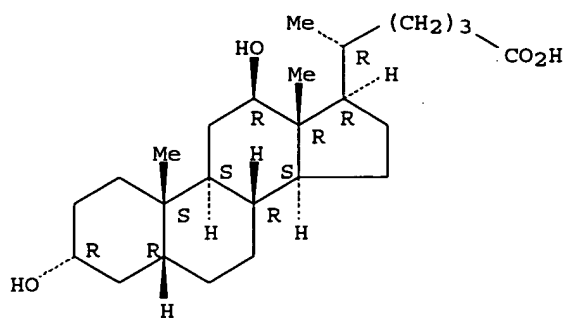
Absolute stereochemistry.



RN 153311-80-9 HCAPLUS

CN Cholan-24-carboxylic acid, 3,12-dihydroxy-, (3 $\alpha$ ,5 $\beta$ ,12 $\beta$ )-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1992:546478 HCAPLUS  
 DN 117:146478  
 ED Entered STN: 17 Oct 1992  
 TI Bile acids and conjugates identified in metabolic disorders by  
 fast atom bombardment and tandem mass spectrometry  
 AU Libert, Raymond; Hermans, Dominique; Draye, Jean Pierre; Van Hoof,  
 Francois; Sokal, Etienne; De Hoffmann, Edmond  
 CS Dep. Neuropediatrics, Clin. Univ. St. Luc, Brussels, B-1200, Belg.  
 SO Clinical Chemistry (Washington, DC, United States) (1991),  
 37(12), 2102-10  
 CODEN: CLCHAU; ISSN: 0009-9147  
 DT Journal  
 LA English  
 CC 9-5 (Biochemical Methods)  
 Section cross-reference(s): 14, 73, 80  
 AB From a study of the collision-activated fragmentation of bile acids, a  
 qual. anal. method based on neg.-ion fast-atom-bombardment (FAB) tandem  
 mass spectrometry was developed. The times for sample preparation and analyses  
 are short. Both free and conjugated bile acids are detected as  
 they occur in biol. fluids, acids are detected as they occur in biol.  
 fluids, without derivatization. For identifying bile acids and  
 conjugates, the method offers better specificity and sensitivity  
 than does the fast atom bombardment mass spectrometric technique alone.  
 Specific scan modes were developed for the selective detection of taurine  
 conjugates,  $\Delta^4$ -unsatd. taurine conjugates,  
 $\Delta^4$ -3-keto free acids and their glycine conjugates, free  
 acids and glycine conjugates bearing a hydroxyl group at the  
 C-12 position, sulfates of glycine and taurine conjugates, and a  
 C29 dicarboxylic bile acid, specific for generalized peroxisomal  
 disorders. Applications of this technique demonstrate its potential  
 usefulness, principally in the diagnosis of several peroxisomal disorders.  
 ST body fluid bile acid conjugate detection; peroxisome disorder  
 diagnosis bile acid; mass spectrometry bile acid diagnosis  
 IT Bile  
 Blood analysis  
 Urine analysis  
 (bile acids and their conjugates detection in human, by  
 fast-atom-bombardment and tandem mass spectrometry)  
 IT Body fluid  
 (bile acids and their conjugates detections in, by  
 fast-atom-bombardment and tandem mass spectrometry)  
 IT Bile acids  
 Bile salts  
 RL: ANT (Analyte); ANST (Analytical study)  
 (detection of, in biol. fluids by fast-atom-bombardment tandem mass  
 spectrometry, in metabolic disorder diagnosis)  
 IT Mass spectra  
 (of bile acids and their conjugates)  
 IT Bile acids

RL: ANT (Analyte); ANST (Analytical study)  
 (conjugates, detection of, in biol. fluids by  
 fast-atom-bombardment tandem mass spectrometry, in metabolic disorder  
 diagnosis)

IT Peroxisome  
 (disease, diagnosis of, bile acid detection in body fluids by mass  
 spectrometry in)

IT Animal metabolism  
 (disorder, diagnosis of, bile acid detection in human body fluid by  
 mass spectrometry in)

IT Bile acids  
 RL: ANT (Analyte); ANST (Analytical study)  
 (sulfates, detection of, in biol. fluids by fast-atom-bombardment  
 tandem mass spectrometry, in metabolic disorder diagnosis)

IT 516-35-8 640-79-9 13587-11-6 117590-83-7 129944-49-6 143380-61-4  
 143380-62-5 143380-63-6 143442-55-1 143476-63-5  
 143477-50-3  
 RL: ANT (Analyte); ANST (Analytical study)  
 (detection of, in biol. fluid by mass spectrometry)

IT 56-40-6, Glycine, analysis 81-24-3, Taurocholic acid 81-25-4  
 108-88-3D, Toluene, bile acid conjugates 474-25-9 475-31-0,  
 Glycocholic acid 68714-85-2 68756-88-7 117590-89-3 129944-53-2  
 143380-64-7 143384-75-2 143442-56-2 143442-57-3 143476-45-3  
 143476-62-4  
 RL: ANT (Analyte); ANST (Analytical study)  
 (detection of, in biol. fluids by mass spectrometry)

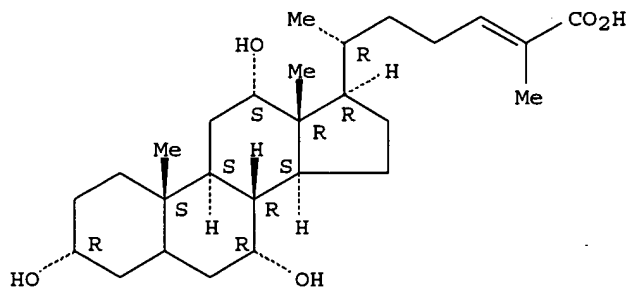
IT 60-18-4, L-Tyrosine, analysis  
 RL: ANST (Analytical study)  
 (metabolic disorders, tyrosine of, type 1, diagnosis of, by bile acid  
 mass spectrometry)

IT 143442-55-1  
 RL: ANT (Analyte); ANST (Analytical study)  
 (detection of, in biol. fluid by mass spectrometry)

RN 143442-55-1 HCAPLUS

CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-,  
 (3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



L40 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1990:421765 HCAPLUS  
 DN 113:21765  
 ED Entered STN: 21 Jul 1990  
 TI Bile acid profiles in peroxisomal 3-oxoacyl-coenzyme A thiolase deficiency  
 AU Clayton, Peter T.; Patel, Ella; Lawson, Alexander M.; Carruthers, Robert  
 A.; Collins, Janna  
 CS Dep. Child Health, Inst. Child Health, London, WC1N 1EH, UK  
 SO Journal of Clinical Investigation (1990), 85(4), 1267-73  
 CODEN: JCINAO; ISSN: 0021-9738  
 DT Journal  
 LA English

CC 14-14 (Mammalian Pathological Biochemistry)

AB Fast atom bombardment mass spectrometry and gas chromatog.-mass spectrometry were used to analyze bile acids in the body fluids of an infant (L.C.) whose liver contained no immunoreactive peroxisomal 3-oxoacyl-CoA thiolase. The profiles were compared with those of six patients with undetectable peroxisomes (Zellweger syndrome) and two siblings (N.B. and I.B.) whose defect of peroxisomal  $\beta$ -oxidation could not be localized by morphol. studies of peroxisomes or by immunoblotting of peroxisomal  $\beta$ -oxidation proteins.  $3\alpha,7\alpha,12\alpha$ -Trihydroxy- $5\beta$ -cholestan-26-oic acid (THCA) was present in bile and plasma of all patients. However, bile from L.C., N.B. and I.B. contained unconjugated varanic acid ( $3\alpha,7\alpha,12\alpha,24$ -tetrahydroxy- $5\beta$ -cholestan-26-oic acid) as the major C27 bile acid, whereas bile from Zellweger patients contained only small amts. of varanic acid. In the bile from L.C. two isomers of varanic acid were present; in the bile from N.B. and I.B. a single isomer predominated. L.C., N.B., and I.B. all produced bile containing small amts. of (24E)- $3\alpha,7\alpha,12\alpha$ -trihydroxy- $5\beta$ -cholest-24-en-26-oic acid ([24E]- $\Delta$ 24-THCA), its [24Z]-isomer,  $3\alpha,7\alpha,12\alpha$ -trihydroxy- $5\beta$ -cholest-23-en-26-oic acid and  $3\alpha,7\alpha,12\alpha$ -trihydroxy-27-nor- $5\beta$ -cholestan-24-one. The results provide evidence for peroxisomal pathways for cholic acid synthesis in man via THCA,  $\Delta$ 24-THCA, and varanic acid and show that bile acid analyses can be used to diagnose peroxisomal thiolase deficiency.

ST bile acid profile oxoacylCoA thiolase deficiency

IT Blood plasma

Urine  
(bile acid profiles of, in peroxisomal oxoacyl-CoA thiolase deficiency of humans, diagnosis in relation to)

IT Body fluid  
(duodenal, bile acid profiles of, in diagnosis of peroxisomal oxoacyl-CoA thiolase deficiency of humans)

IT Bile acids  
RL: BIOL (Biological study)  
(of body fluids, in peroxisomal oxoacyl-CoA thiolase deficiency of humans, diagnosis in relation to)

IT Peroxisome  
(oxoacyl-CoA thiolase deficiency of, bile acid profiles of body fluids in diagnosis of, of humans)

IT 9029-97-4, 3-Oxoacyl-CoA thiolase  
RL: BIOL (Biological study)  
(deficiency of, bile acid profiles of duodenal juice in diagnosis of, of humans)

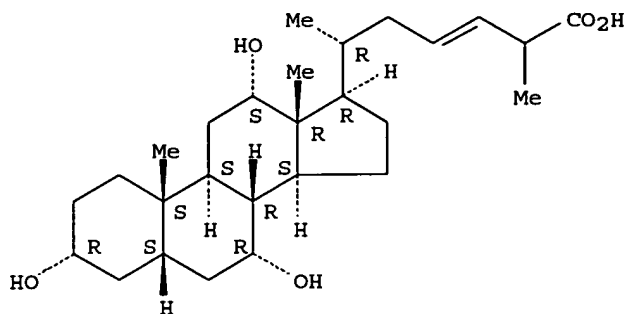
IT 81-25-4, Cholic acid 128-13-2, Ursodeoxycholic acid 474-25-9, Chenodeoxycholic acid 547-98-8 1061-64-9 61628-32-8 72883-89-7 73834-17-0 84888-63-1 85552-38-1 85552-39-2 85552-42-7  
RL: BIOL (Biological study)  
(of duodenal juice, in peroxisomal oxoacyl-CoA thiolase deficiency of humans, diagnosis in relation to)

IT 84888-63-1 85552-38-1 85552-39-2  
RL: BIOL (Biological study)  
(of duodenal juice, in peroxisomal oxoacyl-CoA thiolase deficiency of humans, diagnosis in relation to)

RN 84888-63-1 HCAPLUS

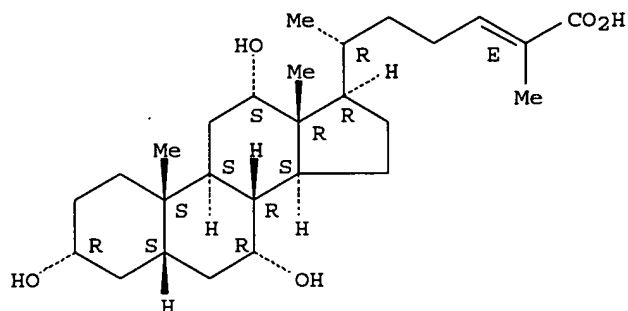
CN Cholest-23-en-26-oic acid,  $3,7,12$ -trihydroxy-, ( $3\alpha,5\beta,7\alpha,12\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



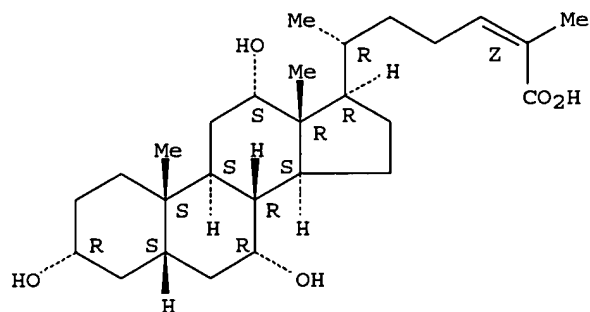
RN 85552-38-1 HCAPLUS  
 CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-,  
 (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ ,24E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



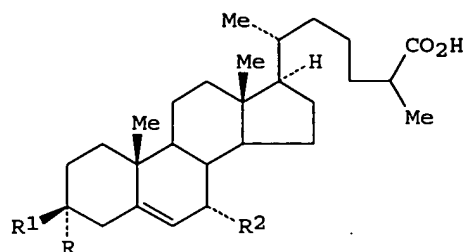
RN 85552-39-2 HCAPLUS  
 CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-,  
 (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ ,24Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L40 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1988:471021 HCAPLUS  
 DN 109:71021  
 ED Entered STN: 02 Sep 1988  
 TI Occurrence of 3 $\beta$ -hydroxy-5-cholestenoic acid, 3 $\beta$ ,7 $\alpha$ -  
 dihydroxy-5-cholestenoic acid, and 7 $\alpha$ -hydroxy-3-oxo-4-cholestenoic  
 acid as normal constituents in human blood  
 AU Axelson, Magnus; Moerk, Birgitta; Sjoevall, Jan

CS Dep. Clin. Chem., Karolinska Hosp., Stockholm, 104 01, Swed.  
 SO Journal of Lipid Research (1988), 29(5), 629-41  
 CODEN: JLPRAW; ISSN: 0022-2275  
 DT Journal  
 LA English  
 CC 13-5 (Mammalian Biochemistry)  
 GI



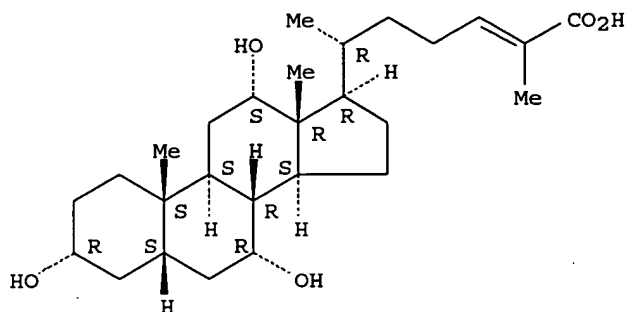
I,  $R=R^2=H$ ,  $R^1=OH$   
 II,  $R=H$ ,  $R^1=R^2=OH$   
 III,  $RR^1=O$ ,  $R^2=OH$

AB Three unconjugated C27 bile acids were found in plasma from healthy humans. They were isolated by liquid-solid extraction and anion-exchange chromatog. and were identified by gas-liquid chromatog.-mass spectrometry, microchem. reactions, and UV spectroscopy as 3 $\beta$ -hydroxy-5-cholestenoic, 3 $\beta$ ,7 $\alpha$ -dihydroxy-5-cholestenoic, and 7 $\alpha$ -hydroxy-3-oxo-4-cholestenoic acids (I, II, and III, resp.). Their levels often exceeded those of the unconjugated C24 bile acids and the variations between individuals were smaller than for the C24 acids. The concns. in plasma from healthy subjects were 67.2 ng/mL for I, 38.9 ng/mL for II, and 81.7 ng/mL for III. The levels of the individual acids were pos. correlated with each other and not with the levels of the C24 acids. The cholestenoic acids were below the detection limit (20-50 ng/mL) in bile, and C27 bile acids present in bile were not detected in plasma.

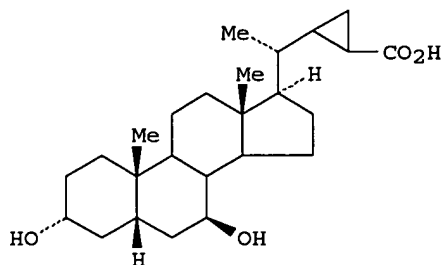
ST cholestenoic acid deriv blood plasma; bile acid C27 blood plasma  
 IT Feeding  
 (bile acids of blood plasma of human response to)  
 IT Bile  
 Blood plasma  
 (bile acids of, of human)  
 IT Bile acids  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (of bile, of human, bile acids of blood plasma in relation to)  
 IT Bile acids  
 RL: BIOL (Biological study)  
 (of blood plasma of human)  
 IT 81-25-4, Cholic acid 474-25-9, Chenodeoxycholic acid 547-98-8  
 5226-26-6 60696-62-0, Norcholic acid 72883-89-7 73804-37-2  
 73834-17-0, 3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ ,26-Tetrahydroxy-5 $\beta$ -cholestan-27-oic acid 73837-07-7  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (of bile, of human)  
 IT 6561-58-6 115538-84-6 115538-85-7  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (of blood plasma, of human)  
 IT 115567-29-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (oxidation of)  
 IT 115538-86-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 5226-26-6  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (of bile, of human)  
 RN 5226-26-6 HCAPLUS  
 CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-,  
 (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



L40 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1988:187048 HCAPLUS  
 DN 108:187048  
 ED Entered STN: 28 May 1988  
 TI Bile acids with a cyclopropyl-containing side chain. 3. Separation, identification, and properties of all four stereoisomers of 3 $\alpha$ ,7 $\beta$ -dihydroxy-22,23-methylene-5 $\beta$ -cholan-24-oic acid  
 AU Pellicciari, Roberto; Natalini, Benedetto; Cecchetti, Sergio; Porter, Barry; Roda, Aldo; Grigolo, Brunella; Balducci, Renzo  
 CS Ist. Chim. Farm. Tec. Farm., Univ. Studi, Perugia, 06100, Italy  
 SO Journal of Medicinal Chemistry (1988), 31(4), 730-6  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DT Journal  
 LA English  
 CC 32-6 (Steroids)  
 OS CASREACT 108:187048  
 GI



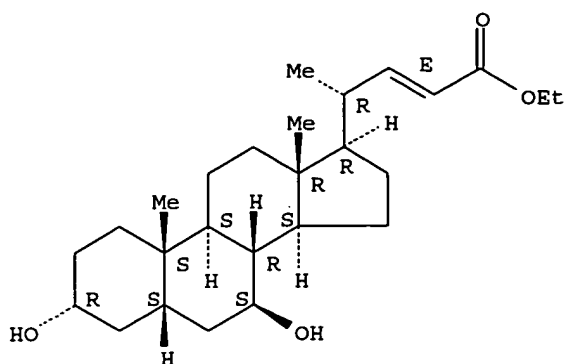
I

AB The 22,23-methylene-5 $\beta$ -cholan-24-oic acid I (CUDCA), a side-chain cyclopropyllog of ursodeoxycholic acid (UDCA), was shown to be a mixture of four stereoisomers (CUDCA A-D). The 22S,23S, 22R,23R, 22S,23R, and 22R,23S diastereoisomers were separated, their resp. configurations assigned by <sup>13</sup>C NMR spectroscopy, and original synthetic schemes for their preparation elaborated. Theor. models of the structure of UDCA and CUDCA A-D were built by using mol. computer graphic techniques. The four diastereoisomers greatly differ in hydrophilicity, in critical micellar

concentration in water, and exhibit a different interaction with intestinal bacterial enzymes. CUDCA A-C are not conjugated with glycine or taurine in the liver, while CUDCA D is secreted into bile predominantly as taurine and glycine conjugate.

- ST methylencholanoic acid stereoisomer configuration; cholanic acid methylene stereoisomer configuration; bile acid biol activity diastereoisomer
- IT Molecular structure-biological activity relationship  
(of 3 $\alpha$ , 7 $\beta$ -dihydroxy-22,23-methylene-5 $\beta$ -cholan-24-oic acid diastereomers)
- IT 105360-63-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyclopropanation of, with Et diazoacetate)
- IT 128-13-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(esterification of)
- IT 113181-05-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and acetylation of)
- IT 113218-62-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and addition reaction with Et diazoacetate)
- IT 113181-08-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and attempted cyclopropanation of)
- IT 113299-41-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and conversion into acetylene derivative)
- IT 113181-06-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and cyclopropanation with diazomethane)
- IT 113181-04-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and elimination reaction of)
- IT 113181-07-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and hydrogenation of)
- IT 69519-36-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and phenylselenylation of)
- IT 89414-90-4P 89495-32-9P 89495-33-0P 89495-34-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and saponification of)
- IT 91378-92-6P 91423-31-3P 91423-32-4P 91423-33-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation, purification, configuration, and biol. activity of)
- IT 113181-05-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and acetylation of)
- RN 113181-05-8 HCAPLUS
- CN Chol-22-en-24-oic acid, 3,7-dihydroxy-, ethyl ester,  
(3 $\alpha$ , 5 $\beta$ , 7 $\beta$ , 22E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L40 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 1987:154139 HCAPLUS  
DN 106:154139  
ED Entered STN: 15 May 1987  
TI Identification of unconjugated bile acids in human bile  
AU Matoba, Naoyuki; Une, Mizuho; Hoshita, Takahiko  
CS Fac. Med., Kyushu Univ., Maidashi, 3-1-1, Japan  
SO Journal of Lipid Research (1986), 27(11), 1154-62  
CODEN: JLPRAW; ISSN: 0022-2275  
DT Journal  
LA English  
CC 14-7 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 13  
AB Unconjugated bile acids in the bile of healthy and diseased (cerebrotendinous xanthomatosis) humans were determined qual. and quant. by gas-liquid chromatog. and gas-liquid chromatog.-mass spectrometry, after their isolation by ion-exchange chromatog. In a healthy person and 3 patients with cholelithiasis, unconjugated bile acids comprised 0.1-0.4% of total biliary bile acids. The bile acid composition of the unconjugated fraction was quite different from that of the glycine- or taurine-conjugate fraction, in that it contained a relatively large proportion of unusual bile acids including C23 and C27 bile acids. In 2 patients with cerebrotendinous xanthomatosis, C22 and C23 bile acids were the major constituents of the biliary unconjugated bile acids and comprised about 0.8% of total bile acids; no detectable amts. of C27 bile acids were found in their bile. The anal. of biliary unconjugated bile acids may be useful for the diagnosis of metabolic diseases concerning bile acids, particularly those diseases which involve the accumulation or disappearance of unusual bile acids.  
ST bile acid bile cholelithiasis cerebrotendinous xanthomatosis  
IT Calculi, biliary  
(unconjugated bile acids of bile in, in humans)  
IT Bile  
(unconjugated bile acids of, of humans)  
IT Bile acids  
RL: BIOL (Biological study)  
(unconjugated, of bile in cerebrotendinous xanthomatosis and cholelithiasis and health in humans)  
IT Xanthomatosis  
(cerebrotendinous, unconjugated bile acids of bile in, in humans)  
IT 56-40-6, biological studies 107-35-7, Taurine  
RL: BIOL (Biological study)  
(bile acids conjugated with, of bile in cerebrotendinous xanthomatosis and cholelithiasis and health in humans)  
IT 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 128-13-2, Ursodeoxycholic acid 474-25-9, Chenodeoxycholic acid 547-98-8

911-40-0, 7-Ketodeoxycholic acid 2464-18-8, Allocholic acid 2955-27-3,  
 7-Epicholic acid 38917-20-3 60696-62-0, Norcholic acid 61844-74-4  
 73804-37-2 73834-17-0 73837-07-7 85552-39-2 86386-61-0  
 98349-18-9 99697-24-2 107480-95-5

RL: BIOL (Biological study)

(unconjugated, of bile in cerebrotendinous xanthomatosis and  
 cholelithiasis and health in humans)

IT 85552-39-2 107480-95-5

RL: BIOL (Biological study)

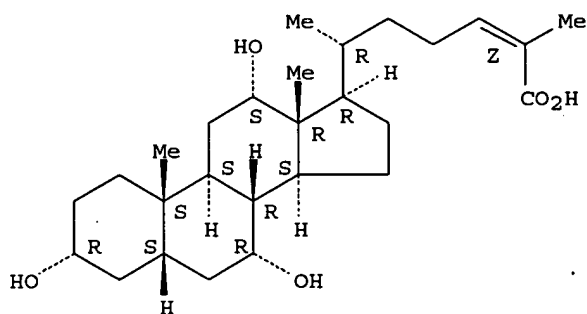
(unconjugated, of bile in cerebrotendinous xanthomatosis and  
 cholelithiasis and health in humans)

RN 85552-39-2 HCAPLUS

CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-,  
 (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ ,24Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

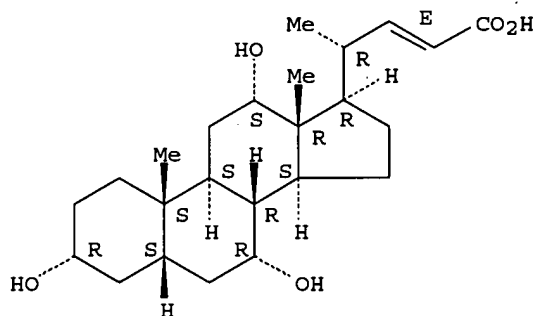


RN 107480-95-5 HCAPLUS

CN Chol-22-en-24-oic acid, 3,7,12-trihydroxy-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12.  
 alpha.,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



=> b embase

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 substance identification.

Search done by Noble Jarrell

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L48 ANSWER 1 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 2004197875 EMBASE

TI Absorption of the cholic acid-conjugated peptide hormone cholysecretin from the rat ileum in vivo.

AU McHarg S.; Morton J.S.; McGinn B.J.; Yasin M.; Morrison J.D.

CS J.D. Morrison, West Medical Building, University of Glasgow, Glasgow G12 8QQ, United Kingdom

SO Acta Physiologica Scandinavica, (2004) Vol. 181, No. 1, pp. 23-34.  
Refs: 29  
ISSN: 0001-6772 CODEN: APSCAX

CY United Kingdom

DT Journal; Article

FS 003 Endocrinology  
030 Pharmacology  
037 Drug Literature Index  
048 Gastroenterology

LA English

SL English

ED Entered STN: 20040610  
Last Updated on STN: 20040610

AB Aims: Previously, we demonstrated that gastrin peptides as long as 34 amino acids were absorbed from the ileum of rat after conjugation to the C24 position of cholic acid and that these peptides retained full biological activity. As absorption was specific to the ileum, it was inferred that the conjugated hormone was taken up by the bile salt transporters. We have now extended these experiments to a member of a different family of hormones, viz. secretin, a 27-amino acid hormone that stimulates serous secretions from the exocrine pancreas. Methods: After conjugation to cholic acid, the degree of cholysecretin absorption from the ileum of anaesthetized rats was assessed from the increase in pancreatic secretions. Results: A complication to the study was that intra-ileal infusion of native secretin caused a transient increase in the levels of pancreatic secretions. This was in contrast to the effects of intra-ileal infusion of cholysecretin which did not cause this transient increase but, instead, gave rise to a delayed increase in pancreatic secretions which was sustained over several hours during which cholysecretin was detected in plasma in high concentration by mass spectrometry. The pancreatic response to cholysecretin was abolished by co-infusion of 50 mM taurocholate, employed to compete with the bile salt transporters, although a transient increase in pancreatic secretions similar to that caused by secretin was now generated. This was shown to arise from an action of taurocholate per se causing the release of endogenous secretin which is present in rat ileum. Conclusions: We, therefore, concluded that cholysecretin had been absorbed from the rat ileum by uptake by bile salt transporters.

CT Medical Descriptors:  
\*hormone release  
\*hormonal regulation  
\*small intestine absorption  
\*ileum  
drug effect  
drug efficacy  
drug mechanism  
pancreas secretion  
hormone blood level  
secretin blood level  
intestine absorption  
pharmacological blocking  
pancreas  
nonhuman  
male  
rat

animal experiment  
 controlled study  
 animal tissue  
 article  
 priority journal  
 Drug Descriptors:  
 \*cholic acid: PD, pharmacology  
 \*secretin: EC, endogenous compound  
 \*secretin: PD, pharmacology  
 recombinant hormone: PD, pharmacology  
 carrier protein: EC, endogenous compound  
 sodium chloride: EC, endogenous compound  
 taurocholic acid: PD, pharmacology  
 RN (cholic acid) 32500-01-9, 361-09-1, 81-25-4;  
 (secretin) 1393-25-5, 17034-35-4, 73559-81-6; (carrier protein)  
 80700-39-6; (sodium chloride) 7647-14-5; (taurocholic acid) 145-42-6,  
 59005-70-8, 81-24-3  
 CO Sigma Aldrich  
  
 L48 ANSWER 2 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 2002415967 EMBASE  
 TI Absorption of biologically active peptide hormones from the small  
 intestine of rat.  
 AU Wheeler S.; McGinn B.J.; Lucas M.L.; Morrison  
 J.D.  
 CS J.D. Morrison, West Medical Building, University of Glasgow, Glasgow G12  
 8QQ, United Kingdom  
 SO Acta Physiologica Scandinavica, (2002) Vol. 176, No. 3, pp. 203-213.  
 Refs: 34  
 ISSN: 0001-6772 CODEN: APSCAX  
 CY United Kingdom  
 DT Journal; Article  
 FS 002 Physiology  
 030 Pharmacology  
 037 Drug Literature Index  
 048 Gastroenterology  
 LA English  
 SL English  
 ED Entered STN: 20021202  
 Last Updated on STN: 20021202  
 AB Absorption of the 4, 10 and 34 amino acid forms of gastrin from the small  
 intestine has been investigated in anaesthetized rats. The method of  
 assessment of successful absorption of the hormone into the systemic  
 circulation was when the amount of acid secreted by the stomach over  
 consecutive 15-min periods was increased. When the natural hormones were  
 infused into the ileum in a relatively high dose, there was no increase in  
 gastric acid secretion, indicating that they had not been absorbed. Each  
 of the forms of gastrin was conjugated at the free amino terminus to the  
 carboxyl group of cholic acid. Subsequent infusion of the conjugated form  
 of gastrin into the ileum, this time in relatively low doses, resulted in  
 substantial and prolonged increases in gastric acid secretion, indicating  
 that these hormones had been successfully absorbed. In addition,  
 conjugation of the 10 and 34 amino acid forms of gastrin with cholic acid  
 was shown to increase markedly the potency in evoking an increase in  
 gastric acid secretion in response to intravenous injection of the  
 hormone. Absorption of the gastrin conjugates was specific to the ileum  
 thus indicating that they had been absorbed through the bile salt  
 transporters.  
 CT Medical Descriptors:  
 \*small intestine absorption  
 systemic circulation  
 acid secretion  
 ileum  
 stomach acid secretion  
 amino terminal sequence

conjugation  
 carboxy terminal sequence  
 drug effect  
 drug megadose  
 nonhuman

male  
 rat  
 animal experiment  
 controlled study  
 animal tissue

article  
 priority journal  
 Drug Descriptors:

\*peptide hormone: DO, drug dose  
 \*peptide hormone: PD, pharmacology  
 \*peptide hormone: IV, intravenous drug administration  
 \*gastrin: DO, drug dose  
 \*gastrin: PD, pharmacology  
 \*gastrin: IV, intravenous drug administration  
 cholic acid

RN (gastrin) 9002-76-0; (cholic acid) 32500-01-9, 361-09-1  
 , 81-25-4

L48 ANSWER 3 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN

AN 91218502 EMBASE

DN 1991218502

TI The effect of sodium deoxycholate and other surfactants on the mucosal  
 surface pH in proximal jejunum or rat.

AU McKie A.T.; Stewart W.; Lucas M.L.

CS Institute of Physiology, Glasgow University, Glasgow G12 8QQ, United  
 Kingdom

SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1991) Vol. 343, No. 6,  
 pp. 659-664.

ISSN: 0028-1298 CODEN: NSAPCC

CY Germany

DT Journal; Article

FS 002 Physiology  
 004 Microbiology  
 029 Clinical Biochemistry  
 048 Gastroenterology  
 052 Toxicology  
 030 Pharmacology  
 037 Drug Literature Index

LA English

SL English

ED Entered STN: 911216

Last Updated on STN: 911216

AB The mucosal surface pH (acid microclimate) and nucleotide levels of rat  
 proximal jejunum were measured in vivo under various conditions which  
 included exposure to pharmacological agents and to surfactants. Mucosal  
 surface pH was unaffected by sodium nitroprusside, A23187 and amiloride,  
 as was mucosal cGMP content, although amiloride and A23187 reduced cAMP  
 content. In contrast, surfactants elevated the pH of the mucosal surface  
 significantly ( $P < 0.001$ ): control value  $6.23 \pm 0.02$  ( $n = 12$ ); Lubrol  
 PX 0.8% (v/v)  $6.98 \pm 0.02$  ( $n = 5$ ); sodium deoxycholate 2 mmol/l  $6.67$   
 $\pm 0.04$  ( $n = 5$ ); Triton X-100 0.5% (v/v)  $7.41 \pm 0.03$  ( $n = 5$ ). No  
 significant changes in cGMP levels were noted after surfactant treatment,  
 although DOC and Triton X-100 reduced cAMP levels. The ability of higher  
 concentrations of surfactant to elevate the mucosal surface pH beyond  
 neutrality to values similar to plasma pH contrasts with the action of  
 Escherichia coli heat-stable (STa) enterotoxin which at high  
 concentrations could not elevate the mucosal surface pH beyond neutrality.  
 Consistent with the known effects on tight junction permeability,  
 surfactants may act by allowing plasma-like subepithelial fluid to  
 neutralise the microclimate.

CT Medical Descriptors:  
 \*cell surface  
 \*jejunum mucosa  
 \*ph  
 animal experiment  
 animal tissue  
 article  
 controlled study  
 male  
 microscopy  
 nonhuman  
 priority journal  
 radioimmunoassay  
 rat  
 regional perfusion  
 Drug Descriptors:  
 \*amiloride: PD, pharmacology  
 \*calcimycin: PD, pharmacology  
 \*cyclic gmp: EC, endogenous compound  
 \*deoxycholate sodium: TO, drug toxicity  
 \*nitroprusside sodium: PD, pharmacology  
 \*surfactant: TO, drug toxicity  
 cyclic amp: EC, endogenous compound  
 docusate sodium: TO, drug toxicity  
 escherichia coli enterotoxin: TO, drug toxicity  
 lubrol: TO, drug toxicity  
 triton x 100: TO, drug toxicity  
 RN (amiloride) 2016-88-8, 2609-46-3; (calcimycin) 52665-69-7; (cyclic gmp) 7665-99-8; (deoxycholate sodium) 302-95-4; (nitroprusside sodium) 14402-89-2, 15078-28-1; (cyclic amp) 60-92-4; (docusate sodium) 577-11-7; (lubrol) 11138-41-3, 52434-01-2  
 CN Lubrol px; Triton x 100; A 23187  
 L48 ANSWER 4 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 83183463 EMBASE  
 DN 1983183463  
 TI The effect of deoxycholate on intestinal surface pH and 5-methyltetrahydropteroylglutamate absorption in the rat proximal jejunum in vitro.  
 AU Blair J.A.; Hilburn M.E.; Lucas M.L.; Said H.M.  
 CS Dep. Chem., Univ. Aston Birmingham, Birmingham B4 7ET, United Kingdom  
 SQ Biochemical Society Transactions, (1983) Vol. 11, No. 2, pp. 165-167.  
 CODEN: BCSTB5  
 CY United Kingdom  
 DT Journal  
 FS 037 Drug Literature Index  
 029 Clinical Biochemistry  
 002 Physiology  
 048 Gastroenterology  
 LA English  
 ED Entered STN: 911209  
 Last Updated on STN: 911209  
 CT Medical Descriptors:  
 \*5 methyltetrahydrofolic acid c 14  
 \*drug absorption  
 \*intestine absorption  
 \*intestine mucosa  
 \*ph  
 jejunum  
 nonhuman  
 rat  
 small intestine  
 animal cell  
 digestive system  
 Drug Descriptors:

\*5 methyltetrahydrofolic acid  
 \*deoxycholic acid  
 radioisotope  
 RN (5 methyltetrahydrofolic acid) 134-35-0; (deoxycholic acid)  
 83-44-3

=> d all 151 tot

L51 ANSWER 1 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 1999324376 EMBASE  
 TI Study of the pharmacological effect of the bile salt, sodium scymnol  
 sulfate, from Rhizoprionodon acutus. IV. Effects of naturally occurring  
 bile alcohols, bile acids and their conjugates on lesion  
 development and vascular endothelial cell injury in a rat peripheral  
 arterial occlusion model.  
 AU Ishida H.; Nakayasu H.; Tsuji K.  
 CS H. Ishida, School of Pharmaceutical Science, University of Shizuoka, 52-1  
 Yada, Shizuoka 422-8526, Japan  
 SO Biological and Pharmaceutical Bulletin, (1999) Vol. 22, No. 8, pp.  
 828-835.  
 Refs: 48  
 ISSN: 0918-6158 CODEN: BPBLEO  
 CY Japan  
 DT Journal; Article  
 FS 018 Cardiovascular Diseases and Cardiovascular Surgery  
 030 Pharmacology  
 037 Drug Literature Index  
 LA English  
 SL English  
 ED Entered STN: 19990930  
 Last Updated on STN: 19990930  
 AB A series of naturally occurring bile alcohols, bile acids and their  
 conjugates has been investigated as part of our studies to develop  
 unique anticoagulants with a potent prophylactic effect against vascular  
 endothelial cell injury induced by lactic acidosis in vivo and in vitro.  
 In an in vivo rat peripheral arterial occlusion model induced by lactic  
 acid injection, oral administration of a single dose of 3 mg/kg scymnol  
 significantly inhibited edematous swelling and development of lower limb  
 lesions, including gangrene, and reduced changes in clotting system  
 functions and serum lactate dehydrogenase activity. It had no effect on  
 clotting system functions in sham-operated rats. The structure-activity  
 relationship suggests that the [24R-(+)-5 $\beta$ -cholestane-  
 3 $\alpha$ ,7 $\alpha$ ,24,26-pentol] or [3 $\alpha$ ,7 $\alpha$ -dihydroxy-5 $\beta$ -  
 cholanolic acid] structure is important for a potent prophylactic effect  
 following oral administration. Intravenous administration of a single  
 dose of 0.3 mg/kg sodium (25S)-scymnol sulfate or scymnol prevented lesion  
 progression as effectively as oral administration of scymnol. Sodium  
 (25S)-scymnol sulfate and ursodeoxycholic acid showed clear protective  
 effects against cultured vascular endothelial cell damage due to lactic  
 acidosis which were dose-dependent. The above results suggest that bile  
 steroids such as scymnol, sodium (25S)-scymnol sulfate, ursodeoxycholic  
 acid, and chenodeoxycholic acid may play a role in protecting endothelial  
 cells against injury caused by lactic acidosis. These compounds are  
 candidates for novel anti-ischemic drugs that act by specifically  
 protecting vascular endothelial cells.  
 CT Medical Descriptors:  
 \*peripheral occlusive artery disease: DT, drug therapy  
 \*peripheral occlusive artery disease: PC, prevention  
 gangrene: PC, prevention  
 structure activity relation  
 lactate dehydrogenase blood level  
 prophylaxis  
 vascular endothelium

cell protection  
 nonhuman  
 male  
 rat  
 animal experiment  
 animal model  
 controlled study  
 animal tissue  
 animal cell  
     oral drug administration  
 intravenous drug administration  
 intraperitoneal drug administration  
 article  
 Drug Descriptors:  
     \*bile salt: DT, drug therapy  
     \*bile acid: DT, drug therapy  
         \*bile acid conjugate: DT, drug therapy  
     \*scymnol: DT, drug therapy  
 lactic acid  
 lactate dehydrogenase: EC, endogenous compound  
 ursodeoxycholic acid: DT, drug therapy  
 argatroban: DT, drug therapy  
 chenodeoxycholic acid: DT, drug therapy  
 cholic acid: DT, drug therapy  
 tauroursodeoxycholic acid: DT, drug therapy  
 taurochenodeoxycholic acid: DT, drug therapy  
 taurocholic acid: DT, drug therapy  
 RN (lactic acid) 113-21-3, 50-21-5; (lactate dehydrogenase) 9001-60-9;  
 (ursodeoxycholic acid) 128-13-2, 2898-95-5;  
 (argatroban) 74863-84-6; (chenodeoxycholic acid) 474-25-9;  
 (cholic acid) 32500-01-9, 361-09-1, 81-25-4;  
 (tauroursodeoxycholic acid) 14605-22-2; (taurochenodeoxycholic acid)  
 516-35-8; (taurocholic acid) 145-42-6, 59005-70-8, 81-24-3  
 CO Wako; Tokyo Tanabe; Sigma; Daiichi Pharmaceutical (Japan)  
 L51 ANSWER 2 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 1999256785 EMBASE  
 TI Simultaneous determination of ursodeoxycholic acid and its glycine-  
 conjugate in serum as phenacyl esters using multidimensional  
 liquid chromatography.  
 AU Choi S.J.; Jeong C.K.; Lee H.M.; Kim K.; Do K.S.; Lee H.S.  
 CS S.J. Choi, College of Pharmacy, Wonkwang University, Iksan 570-749, Korea,  
 Republic of  
 SO Chromatographia, (1999) Vol. 50, No. 1-2, pp. 96-100.  
 Refs: 25  
 ISSN: 0009-5893 CODEN: CHRGB7  
 CY Germany  
 DT Journal; Article  
 FS 030 Pharmacology  
 037 Drug Literature Index  
 LA English  
 SL English  
 ED Entered STN: 19990812  
 Last Updated on STN: 19990812  
 AB A narrowbore high-performance liquid chromatographic (HPLC) method using  
 column switching is described for the simultaneous determination of  
 ursodeoxycholic acid (UDCA) and glyco-UDCA (GUDCA) from serum samples as  
 their phenacyl esters. Serum samples were subjected to a preliminary  
 clean-up using octadecylsilane reversed-phase extraction and derivatized  
 with phenacylbromide. The purification, fractionation and concentration  
 of UDCA and GUDCA from the esterified serum sample were performed on-line  
 by appropriate switching of columns. Limit of detection (LOD) of UDCA and  
 GUDCA were 5 ng and the absolute mean recoveries averaged 84.4 ± 8.2%  
 and 85.2 ± 8.4%, respectively. This method was successfully applied  
 to the pharmacokinetic study of UDCA in rats and human.

CT Medical Descriptors:  
 \*high performance liquid chromatography  
 extraction  
 purification  
 fractionation  
 drug blood level  
 validation process  
 human  
 nonhuman  
 rat  
 oral drug administration  
 intravenous drug administration  
 article  
 priority journal  
 Drug Descriptors:  
 \*ursodeoxycholic acid: AD, drug administration  
 \*ursodeoxycholic acid: CR, drug concentration  
 \*ursodeoxycholic acid: DO, drug dose  
 \*ursodeoxycholic acid: PK, pharmacokinetics  
 \*glycine  
 \*ester derivative  
 \*glycoursodeoxycholic acid  
 silane derivative  
 bromine derivative  
 RN (ursodeoxycholic acid) 128-13-2, 2898-95-5; (glycine)  
 56-40-6, 6000-43-7, 6000-44-8; (glycoursodeoxycholic acid)  
 64480-66-6  
 CO Sigma (United States)

L51 ANSWER 3 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 1999046272 EMBASE  
 TI Inhibition of protein denaturation by fatty acids, bile salts and other  
 natural substances: A new hypothesis for the mechanism of action of fish  
 oil in rheumatic diseases.  
 AU Saso L.; Valentini G.; Casini M.L.; Mattei E.; Braghiroli L.; Mazzanti G.;  
 Panzironi C.; Grippa E.; Silvestrini B.  
 CS B. Silvestrini, Inst. Pharmacology and Pharmacognosy, University 'La  
 Sapienza', P.le Aldo Moro 5, 00185 Rome, Italy  
 SO Japanese Journal of Pharmacology, (1999) Vol. 79, No. 1, pp. 89-99.  
 Refs: 41  
 ISSN: 0021-5198 CODEN: JJPAAZ  
 CY Japan  
 DT Journal; Article  
 FS 017 Public Health, Social Medicine and Epidemiology  
 026 Immunology, Serology and Transplantation  
 029 Clinical Biochemistry  
 030 Pharmacology  
 031 Arthritis and Rheumatism  
 037 Drug Literature Index  
 LA English  
 SL English  
 ED Entered STN: 19990218  
 Last Updated on STN: 19990218  
 AB Natural hydrophobic substances like bile salts (cholate, deoxycholate,  
 chenodeoxycholate, lithocholate and their conjugates with  
 glycine and taurine), fatty acids (caprylic, capric, lauric, myristic,  
 palmitic, stearic, oleic, linoleic, arachidonic, eicosapentaenoic and  
 docosahexaenoic acid) were much more active (EC50 .simeq. 10-4-10-5 M)  
 than selected amino acids (EC50 > 10-2 M) and inorganic salts (EC50  
 .simeq. 10-1 M) in inhibiting heat-induced denaturation of human serum  
 albumin in vitro. Fish oil, rich in n-3-polyunsaturated acids such as  
 eicosapentaenoic acid and docosahexaenoic acid, administered p.o. (1  
 ml/kg) in the rat, protected ex vivo (after 2 hr) serum against  
 heat-induced denaturation more than bendazac, a known antidenaturant drug.  
 Thus, we speculated that the antidenaturant activity of fish oil may be

partly (in addition to the known effect on endogenous eicosanoid composition) responsible for its beneficial effects in rheumatoid arthritis and other rheumatic conditions. In this connection, it is of note that the in vitro antidenaturant activity of fish oil fatty acids was higher than that of known antidenaturant drugs such as bendazac and bindarit and nonsteroidal anti-inflammatory drugs like phenylbutazone and indomethacin which could exert beneficial effects in chronic inflammatory conditions by stabilizing endogenous proteins.

CT

## Medical Descriptors:

- \*protein denaturation
- \*drug mechanism
- \*rheumatic disease: DT, drug therapy
- protein stability
- cattle
- human
- nonhuman
- rat
- normal human
- animal experiment
- controlled study
- human tissue
- animal tissue

- oral drug administration

## article

## Drug Descriptors:

- \*fatty acid: DV, drug development
- \*fatty acid: PD, pharmacology
- \*fish oil: DV, drug development
- \*fish oil: DT, drug therapy
- \*fish oil: PD, pharmacology
- \*bile salt: DV, drug development
- \*bile salt: PD, pharmacology
- cholic acid: CM, drug comparison
- cholic acid: DV, drug development
- cholic acid: PD, pharmacology
- deoxycholic acid: CM, drug comparison
- deoxycholic acid: DV, drug development
- deoxycholic acid: PD, pharmacology
- chenodeoxycholic acid: CM, drug comparison
- chenodeoxycholic acid: DV, drug development
- chenodeoxycholic acid: PD, pharmacology
- lithocholic acid: CM, drug comparison
- lithocholic acid: DV, drug development
- lithocholic acid: PD, pharmacology
- bile acid conjugate: CM, drug comparison
  - bile acid conjugate: DV, drug development
  - bile acid conjugate: PD, pharmacology
- octanoic acid: CM, drug comparison
- octanoic acid: DV, drug development
- octanoic acid: PD, pharmacology
- decanoic acid: CM, drug comparison
- decanoic acid: DV, drug development
- decanoic acid: PD, pharmacology
- lauric acid: CM, drug comparison
- lauric acid: DV, drug development
- lauric acid: PD, pharmacology
- myristic acid: CM, drug comparison
- myristic acid: DV, drug development
- myristic acid: PD, pharmacology
- palmitic acid: CM, drug comparison
- palmitic acid: DV, drug development
- palmitic acid: PD, pharmacology
- stearic acid: CM, drug comparison
- stearic acid: DV, drug development
- stearic acid: PD, pharmacology
- oleic acid: CM, drug comparison

oleic acid: DV, drug development  
 oleic acid: PD, pharmacology  
 linoleic acid: CM, drug comparison  
 linoleic acid: DV, drug development  
 linoleic acid: PD, pharmacology  
 arachidonic acid: CM, drug comparison  
 arachidonic acid: DV, drug development  
 arachidonic acid: PD, pharmacology  
 icosapentaenoic acid: CM, drug comparison  
 icosapentaenoic acid: DV, drug development  
 icosapentaenoic acid: PD, pharmacology  
 docosahexaenoic acid: CM, drug comparison  
 docosahexaenoic acid: DV, drug development  
 docosahexaenoic acid: PD, pharmacology  
 amino acid: CM, drug comparison  
 amino acid: DV, drug development  
 amino acid: PD, pharmacology  
 inorganic salt: CM, drug comparison  
 inorganic salt: DV, drug development  
 inorganic salt: PD, pharmacology  
 human serum albumin  
 omega 3 fatty acid: CM, drug comparison  
 omega 3 fatty acid: DV, drug development  
 omega 3 fatty acid: PD, pharmacology  
 bendazac: CM, drug comparison  
 bindarit: CM, drug comparison  
 phenylbutazone: CM, drug comparison  
 indometacin: CM, drug comparison  
 antirheumatic agent: CM, drug comparison  
 antirheumatic agent: DV, drug development  
 antirheumatic agent: PD, pharmacology  
 glycochenodeoxycholic acid: CM, drug comparison  
 glycochenodeoxycholic acid: DV, drug development  
 glycochenodeoxycholic acid: PD, pharmacology  
 unindexed drug  
 unclassified drug

- RN (fish oil) 8016-13-5; (cholic acid) 32500-01-9, 361-09-1  
 , 81-25-4; (deoxycholic acid) 83-44-3;  
 (chenodeoxycholic acid) 474-25-9; (lithocholic acid)  
 434-13-9; (octanoic acid) 124-07-2, 1984-06-1, 74-81-7; (decanoic  
 acid) 334-48-5, 3398-75-2; (lauric acid) 115-05-9, 143-07-7; (myristic  
 acid) 1715-79-3, 544-63-8; (palmitic acid) 57-10-3; (stearic acid)  
 57-11-4, 646-29-7; (oleic acid) 112-80-1, 115-06-0; (linoleic acid)  
 1509-85-9, 2197-37-7, 60-33-3, 822-17-3; (arachidonic acid) 506-32-1,  
 6610-25-9, 7771-44-0; (icosapentaenoic acid) 25378-27-2, 32839-30-8;  
 (docosahexaenoic acid) 25167-62-8, 32839-18-2; (amino acid) 65072-01-7;  
 (human serum albumin) 9048-49-1; (bendazac) 20187-55-7; (phenylbutazone)  
 129-18-0, 50-33-9, 8054-70-4; (indometacin) 53-86-1, 74252-25-8,  
 7681-54-1; (glycochenodeoxycholic acid) 640-79-9  
 CO Sigma (United States); Merck (Germany)
- L51 ANSWER 4 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 96132330 EMBASE  
 DN 1996132330  
 TI Bile acid conjugation in early stage cholestatic liver disease  
 before and during treatment with ursodeoxycholic acid.  
 AU Fracchia M.; Setchell K.D.R.; Crosignani A.; Podda M.; O'Connell N.;  
 Ferraris R.; Hofmann A.F.; Galatola G.  
 CS Divisione di Gastroenterologia, Ospedale Mauriziano Umberto I, Largo  
 Turati, 62, I-10128 Torino, Italy  
 SO Clinica Chimica Acta, (1996) Vol. 248, No. 2, pp. 175-185.  
 ISSN: 0009-8981 CODEN: CCATAR  
 CY Netherlands  
 DT Journal; Article  
 FS 023 Nuclear Medicine

029 Clinical Biochemistry  
 048 Gastroenterology  
 037 Drug Literature Index

LA English  
 SL English  
 ED Entered STN: 960604  
 Last Updated on STN: 960604

AB The efficiency of bile acid conjugation before and during therapy with 600 mg/day of ursodeoxycholic acid was measured in seven adult patients with early chronic cholestatic liver disease (6 with primary biliary cirrhosis; 1 with primary sclerosing cholangitis). Duodenal bile samples were obtained by aspiration and the proportion of unconjugated bile acids was determined using lipophilic anion exchange chromatography to separate bile acid classes, followed by analysis of individual bile acids by gas chromatography-mass spectrometry. The proportion of conjugated bile acids was determined by high-performance liquid chromatography. Use of a  $^{99m}\text{Tc}$ -HIDA recovery marker permitted the absolute mass of unconjugated bile acids in the gallbladder to be calculated. Unconjugated bile acids comprised 0.4% of total biliary bile acids before and 0.2% during ursodeoxycholic acid therapy, indicating highly efficient conjugation of bile acids. During therapy, percentage unconjugated ursodeoxycholic acid significantly increased from (mean  $\pm$  S.D.)  $13 \pm 13\%$  to  $54 \pm 12\%$ ;  $P < 0.002$ . When the unconjugated and conjugated fractions of bile acids were compared, there was an enrichment in unconjugated fraction for cholic acid and ursodeoxycholic acid and a depletion for chenodeoxycholic acid both in basal condition and during ursodeoxycholic acid therapy, suggesting that hydrophilic bile acids were conjugated less efficiently. During therapy, the conjugation efficiency significantly increased for cholic acid and ursodeoxycholic acid. The pretreatment mass of total unconjugated bile acids in the gallbladder was (mean  $\pm$  S.D.)  $4.4 \pm 3.2 \mu\text{mol}$ , and was not significantly changed by ursodeoxycholic acid therapy ( $6.2 \pm 3.5 \mu\text{mol}$ ). However, ursodeoxycholic acid therapy caused a significant increase in the mass of unconjugated ursodeoxycholic acid. It is concluded that endogenous bile acids and exogenous ursodeoxycholic acid when given at the usual dose are efficiently conjugated in patients with early cholestatic liver disease. Despite showing increased biliary unconjugated ursodeoxycholic acid during its oral administration, our data do not lend support to the occurrence of hypercholeremia due to cholehepatic shunting of bile acids.

CT Medical Descriptors:  
 \*cholestasis: DT, drug therapy  
 \*liver disease: DT, drug therapy  
 article  
 bile composition  
 clinical article  
 clinical trial  
 gas chromatography  
 high performance liquid chromatography  
 human  
 intravenous drug administration  
 mass spectrometry  
 oral drug administration  
 priority journal  
 Drug Descriptors:  
 \*bile acid conjugate: EC, endogenous compound  
 \*ursodeoxycholic acid: DT, drug therapy  
 lidofenin tc  $^{99m}$

RN (ursodeoxycholic acid) 128-13-2, 2898-95-5

L51 ANSWER 5 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 95240331 EMBASE  
 DN 1995240331

TI Tauroursodeoxycholate increases rat liver ursodeoxycholate levels and limits lithocholate formation better than ursodeoxycholate.  
 AU Rodrigues C.M.P.; Kren B.T.; Steer C.J.; Setchell K.D.R.  
 CS Department of Pediatrics, Clinical Mass Spectrometry Center, Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229, United States  
 SO Gastroenterology, (1995) Vol. 109, No. 2, pp. 564-572.  
 ISSN: 0016-5085 CODEN: GASTAB  
 CY United States  
 DT Journal; Article  
 FS 037 Drug Literature Index  
 048 Gastroenterology  
 LA English  
 SL English  
 ED Entered STN: 950906  
 Last Updated on STN: 950906  
 AB Background and Aims: To explain the greater hepatoprotective effect of tauroursodeoxycholic acid vs. ursodeoxycholic acid, the absorption, hepatic enrichment, and biotransformation of these bile acids (250 mg/day) were compared in rats. Methods: Bile acids were determined in intestinal contents, feces, urine, plasma, and liver by gas chromatography-mass spectrometry. Results: The concentration of ursodeoxycholate in the liver of animals administered tauroursodeoxycholic acid ( $175 \pm 29$  nmol/g) was greater ( $P < 0.05$ ) than in animals administered ursodeoxycholic acid ( $79 \pm 19$  nmol/g). Hepatic lithocholate was substantially higher after ursodeoxycholic acid administration ( $21 \pm 10$  nmol/g) than after tauroursodeoxycholic acid administration ( $12 \pm 1$  nmol/g). A concomitant reduction in the proportion of hydrophobic bile acids occurred that was greatest during tauroursodeoxycholic acid administration. In the intestinal tract, the mass of ursodeoxycholate and its specific metabolites was greater in rats administered tauroursodeoxycholic acid (27.2 mg) than those administered ursodeoxycholic acid (13.2 mg). In feces, the proportion of lithocholate was  $21.9\% \pm 4.9\%$  and  $5.4\% \pm 4.0\%$  after ursodeoxycholic acid and tauroursodeoxycholic acid administration, respectively. Conclusions: Compared with ursodeoxycholic acid, tauroursodeoxycholic acid induces a greater decrease in the percent composition of more hydrophobic bile acids within the pool, limits lithocholate formation, and increases hepatic ursodeoxycholate concentration. These differences are explained by increased hepatic extraction and reduced intestinal biotransformation and not by enhanced absorption of the amidated species.  
 CT Medical Descriptors:  
 \*bile acid metabolism  
 \*biotransformation  
 \*liver protection  
 amidation  
 animal experiment  
 animal tissue  
 article  
 blood level  
 controlled study  
 drug mechanism  
 feces level  
 gas chromatography  
 hydrophobicity  
 intestine absorption  
 male  
 mass spectrometry  
 nonhuman  
 oral drug administration  
 priority journal  
 rat  
 urine level  
 Drug Descriptors:  
 \*bile acid: EC, endogenous compound  
 \*lithocholic acid: EC, endogenous compound

\*tauroursodeoxycholic acid: CM, drug comparison  
 \*tauroursodeoxycholic acid: PD, pharmacology  
 \*ursodeoxycholic acid: CM, drug comparison  
 \*ursodeoxycholic acid: PD, pharmacology  
 bile acid conjugate: EC, endogenous compound  
 RN (lithocholic acid) 434-13-9; (tauroursodeoxycholic acid)  
 14605-22-2; (ursodeoxycholic acid) 128-13-2, 2898-95-5  
 CO Sigma (United States)

L51 ANSWER 6 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 94299511 EMBASE  
 DN 1994299511  
 TI Effect of a medium dose of ursodeoxycholic acid with or without taurine  
 supplementation on the nutritional status of patients with cystic  
 fibrosis: A randomized, placebo-controlled, crossover trial.  
 AU Merli M.; Bertasi S.; Servi R.; Diamanti S.; Martino F.; De Santis A.;  
 Goffredo F.; Quattrucci S.; Antonelli M.; Angelico M.  
 CS II Cattedra di Gastroenterologia, Viale dell'Universita, 37,00185 Rome,  
 Italy  
 SO Journal of Pediatric Gastroenterology and Nutrition, (1994) Vol. 19, No.  
 2, pp. 198-203.  
 ISSN: 0277-2116 CODEN: JPGND6  
 CY United States  
 DT Journal; Article  
 FS 007 Pediatrics and Pediatric Surgery  
 037 Drug Literature Index  
 048 Gastroenterology  
 LA English  
 SL English  
 ED Entered STN: 941027  
 Last Updated on STN: 941027  
 AB Ursodeoxycholic acid administration has been reported to improve  
 cholestasis and inflammatory activity in primary biliary cirrhosis and, in  
 an uncontrolled study, also in young adults with cystic fibrosis (CF) and  
 chronic cholestasis. As an improvement in nutritional status was also  
 observed in these young adult patients, we investigated whether the  
 administration of a medium dose of ursodeoxycholic acid ameliorates the  
 nutritional status of malnourished young adult CF patients with chronic  
 liver disease. The study included 51 patients (27 male patients and 24  
 female patients; age range, 8-32 years; median, 14) with body mass  
 percentiles <90%. Patients were randomly assigned to receive either  
 ursodeoxycholic acid (10- 12 mg/kg/day) alone or with taurine (18-22  
 mg/kg/day). Patients were followed in a crossover fashion within each  
 group; 6 months of treatment was randomly alternated with 6 months of  
 placebo. Nine patients dropped out before concluding the study. Liver  
 function tests, nutritional status, and coefficients of fat absorption  
 were determined at entry and after each 6 months of placebo or treatment.  
 Nutritional status and fat absorption were not significantly modified by  
 either treatment. Liver function tests improved after ursodeoxycholic  
 acid administration only in patients with concomitant chronic liver  
 disease. Our findings indicate that 6 months of therapy with a medium  
 dose of ursodeoxycholic acid, either alone or with taurine, does not  
 improve the nutritional status of young malnourished CF patients. Higher  
 doses given for longer periods might be worth investigating.

CT Medical Descriptors:  
 \*cholestasis: DT, drug therapy  
 \*cystic fibrosis: CN, congenital disorder  
 \*diet supplementation  
 \*nutritional status  
 adolescent  
 article  
 body mass  
 child  
 clinical trial  
 controlled study

crossover procedure  
 dose response  
 drug efficacy  
 drug mixture  
 enzyme therapy  
 female  
 human  
 lipid absorption  
 liver function test  
 major clinical study  
 male  
 malnutrition: TH, therapy  
 malnutrition: CO, complication  
   oral drug administration  
 pancreas insufficiency: DT, drug therapy  
 pancreas insufficiency: CO, complication  
 priority journal  
 randomized controlled trial  
 Drug Descriptors:  
 \*taurine: DT, drug therapy  
 \*taurine: CB, drug combination  
 \*taurine: CT, clinical trial  
 \*ursodeoxycholic acid: CT, clinical trial  
 \*ursodeoxycholic acid: DT, drug therapy  
 \*ursodeoxycholic acid: DO, drug dose  
 \*ursodeoxycholic acid: CB, drug combination  
 alanine aminotransferase: EC, endogenous compound  
 alkaline phosphatase: EC, endogenous compound  
 amylase: DT, drug therapy  
 amylase: CB, drug combination  
 aspartate aminotransferase: EC, endogenous compound  
   bile acid conjugate: EC, endogenous compound  
 ceruletide  
 ceruletide diethylamine  
 feces lipid  
 gamma glutamyltransferase: EC, endogenous compound  
 pancrelipase: DT, drug therapy  
 placebo  
 tauroursodeoxycholic acid: EC, endogenous compound  
 triacylglycerol lipase: CB, drug combination  
 triacylglycerol lipase: DT, drug therapy  
 trypsin: DT, drug therapy  
 trypsin: CB, drug combination  
 vitamin

RN (taurine) 107-35-7; (ursodeoxycholic acid) 128-13-2,  
 2898-95-5; (alanine aminotransferase) 9000-86-6, 9014-30-6;  
 (alkaline phosphatase) 9001-78-9; (amylase) 9000-90-2, 9000-92-4,  
 9001-19-8; (aspartate aminotransferase) 9000-97-9; (ceruletide)  
 17650-98-5; (ceruletide diethylamine) 71247-25-1; (gamma  
 glutamyltransferase) 85876-02-4; (pancrelipase) 71060-52-1, 83869-36-7;  
 (tauroursodeoxycholic acid) 14605-22-2; (triacylglycerol lipase)  
 9001-62-1; (trypsin) 9002-07-7  
 CN (1) Takus  
 CO (1) Farmitalia carlo erba (Italy)  
 L51 ANSWER 7 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 92292458 EMBASE  
 DN 1992292458  
 TI Effect of ursodeoxycholic acid on the masses of biliary lipids and  
 alkaline phosphatase within the gallbladder in chronic cholestatic liver  
 disease.  
 AU Fracchia M.; Ferraris R.; Petrarulo M.; Secreto P.; Dunn T.; Galatola G.  
 CS Divisione di Gastroenterologia, Ospedale Mauriziano Umberto I, Largo  
 Turati 62,I-10128 Torino, Italy  
 SO European Journal of Gastroenterology and Hepatology, (1992) Vol. 4, No.

10, pp. 843-848.  
 ISSN: 0954-691X CODEN: EJGHES

CY United Kingdom  
 DT Journal; Conference Article  
 FS 030 Pharmacology  
 037 Drug Literature Index  
 048 Gastroenterology

LA English  
 SL English  
 ED Entered STN: 921025  
 Last Updated on STN: 921025

AB Objectives: To verify whether the improvement of the cholestatic indices caused by ursodeoxycholic acid administered for chronic intrahepatic cholestasis is due to a dilution or a removal of the hydrophobic bile acids in the bile. To assess the effect of ursodeoxycholic acid on the masses in the gallbladder of other biliary lipids and alkaline phosphatase. Design: Open prospective study. Methods: Measurement of the masses of total bile acids, bile acid conjugates, cholesterol, phospholipid and alkaline phosphatase within the gallbladder in the fasting state before and after 4-6 weeks of therapy with 600 mg per day oral ursodeoxycholic acid in eight patients with chronic cholestatic liver disease. Results: Ursodeoxycholic acid caused a significant increase in the bile acid mass (from  $1976 \pm 593$  to  $4562 \pm 1474$   $\mu\text{mol}$ ;  $P < 0.02$ ), that was entirely due to an increased mass of its conjugates (from  $35 \pm 20$  to  $1623 \pm 768$   $\mu\text{mol}$ ;  $P < 0.05$ ), whereas the masses of all the other bile acid conjugates were not modified during therapy. In all eight patients, serum alkaline phosphatase concentration decreased during ursodeoxycholic acid therapy, whereas the alkaline phosphatase mass within the gallbladder increased, from  $16 \pm 3$  IU to  $35 \pm 9$  IU ( $P < 0.02$ ). There was no change in the cholesterol and phospholipid masses. Conclusion: Our results indicate that the mechanism of action of ursodeoxycholic acid in chronic intrahepatic cholestasis is not mediated via a reduction of the hydrophobic bile acids handled by the liver, though these are diluted out by ursodeoxycholic acid. The finding of an increased mass of alkaline phosphatase in the gallbladder is probably due to the well known choleretic effect of ursodeoxycholic acid.

CT Medical Descriptors:  
 \*cholestasis: DT, drug therapy  
 \*chronic liver disease: DT, drug therapy  
 \*gallbladder  
 \*lipid bile level  
 adult  
 aged  
 alkaline phosphatase blood level  
 clinical article  
 conference paper  
 female  
 human  
 male  
 oral drug administration  
 primary biliary cirrhosis: DT, drug therapy  
 primary sclerosing cholangitis: DT, drug therapy  
 prospective study  
 Drug Descriptors:  
 \*alkaline phosphatase: EC, endogenous compound  
 \*ursodeoxycholic acid: DT, drug therapy  
 \*ursodeoxycholic acid: PD, pharmacology  
 bile acid conjugate: EC, endogenous compound  
 cholesterol: EC, endogenous compound  
 phospholipid: EC, endogenous compound

RN (alkaline phosphatase) 9001-78-9; (ursodeoxycholic acid) 128-13-2  
 , 2898-95-5; (cholesterol) 57-88-5

CN Deursil  
 CO Labaz (Italy)

L51 ANSWER 8 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 90226900 EMBASE

DN 1990226900

TI Prevention of ursodeoxycholate hepatotoxicity in the rabbit by  
conjugation with N-methyl amino acids.

AU Schmassmann A.; Hofmann A.F.; Angellotti M.A.; Ton-Nu H.-T.; Schteingart  
C.D.; Clerici C.; Rossi S.S.; Rothschild M.A.; Cohen B.I.; Stenger R.J.;  
Mosbach E.H.

CS Lipid Laboratory, Department of Surgery, Beth Israel Medical Center, 10  
Nathan D. Perlman Place, New York, NY 10003, United States

SO Hepatology, (1990) Vol. 11, No. 6, pp. 989-996.  
ISSN: 0270-9139 CODEN: HPTLD

CY United States

DT Journal; Article

FS 048 Gastroenterology  
052 Toxicology  
037 Drug Literature Index

LA English

SL English

ED Entered STN: 911213  
Last Updated on STN: 911213

AB The effect of dietary administration of four different amino acid (N-acyl)  
conjugates of ursodeoxycholic acid on biliary bile acid  
composition, liver tests and hepatic morphology by light microscopy was  
examined in the rabbit. Each group of four to five rabbits received a  
chow diet supplemented with a single conjugate of  
ursodeoxycholic acid ursodeoxycholyl-glycine, ursodeoxycholyl-sarcosine,  
ursodeoxycholyl-taurine or ursodeoxycholyl-N-methyltaurine for 3 wks at a  
dose of 50 mg/kg/day; a control group received chow alone. After 3 wks of  
feeding, animals receiving ursodeoxycholyl-glycine or ursodeoxycholyl-  
taurine had hepatotoxicity associated with abnormal liver tests.  
Lithocholic acid made up  $11\% \pm 2.7\%$  of biliary bile acids in the  
ursodeoxycholyl-glycine and  $10\% \pm 2.2\%$  in the ursodeoxycholyl-  
taurine group. In contrast, animals receiving ursodeoxycholyl-sarcosine or  
ursodeoxycholyl-N-methyltaurine had neither hepatotoxicity nor abnormal  
liver tests and the proportion of lithocholic acid in biliary bile acids  
increased much less. Complementary studies showed that  
ursodeoxycholyl-sarcosine and ursodeoxycholyl-N-methyltaurine were not  
biotransformed during hepatic transport and were resistant to  
deconjugation and dehydroxylation in the rabbit. These  
experiments indicate that the N-methyl amino acid conjugates of  
ursodeoxycholic acid are nontoxic in the rabbit and resist  
deconjugation and dehydroxylation. Such resistance decreases  
formation of lithocholic acid in the colon, thus reducing its accumulation  
and consequent induction of hepatotoxicity.

CT Medical Descriptors:  
\*conjugation  
\*liver toxicity: PC, prevention  
drug conjugation  
rabbit  
animal experiment  
nonhuman  
male  
oral drug administration  
article  
priority journal  
Drug Descriptors:  
\*amino acid  
\*ursodeoxycholic acid: TO, drug toxicity

RN (amino acid) 65072-01-7; (ursodeoxycholic acid) 128-13-2,  
2898-95-5

CO Diamalt aktiengesellschaft (Germany)

L51 ANSWER 9 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 89150062 EMBASE  
 DN 1989150062  
 TI The rapid evaluation of intestinal bacterial growth using a conjugate of ursodeoxycholic acid with para-aminobenzoic acid.  
 AU Maeda Y.; Takahashi M.; Tashiro H.; Akazawa F.  
 CS Department of Pharmacy, Chugoku Rosai Hospital, Hiroshima 737-01, Japan  
 SO Journal of Pharmacobio-Dynamics, (1989) Vol. 12, No. 5, pp. 272-280.  
 ISSN: 0386-846X CODEN: JOPHDQ  
 CY Japan  
 DT Journal  
 FS 030 Pharmacology  
 037 Drug Literature Index  
 LA English  
 ED Entered STN: 911212  
 Last Updated on STN: 911212  
 CT Medical Descriptors:  
 \*bacterial count  
 \*bacterial growth  
 \*blind loop syndrome  
 \*intestine flora  
 animal model  
 choloylglycine hydrolase  
 rat  
 microorganism  
 animal experiment  
 nonhuman  
 male  
 oral drug administration  
 Drug Descriptors:  
 bile acid  
 4 ursodeoxycholamidobenzoic acid  
 clindamycin  
 glycocholic acid  
 kanamycin  
 paromomycin  
 polymyxin b  
 tinidazole  
 vancomycin  
 unclassified drug  
 RN (clindamycin) 18323-44-9; (glycocholic acid) 475-31-0;  
 (kanamycin) 11025-66-4, 61230-38-4, 8063-07-8; (paromomycin) 11035-13-5,  
 1263-89-4, 1390-73-4, 51795-47-2, 54597-56-7, 7542-37-2, 84420-34-8;  
 (polymyxin b) 1404-26-8, 1405-20-5; (tinidazole) 19387-91-8; (vancomycin)  
 1404-90-6, 1404-93-9  
 CO Wako pure chemical industry (Japan); Shionogi (Japan); Upjohn (Japan);  
 Meiji seika kaisha (Japan); Kyowa hakko kogyo (Japan); Pfizer (Japan);  
 Tokyo tanabe (Japan)  
 L51 ANSWER 10 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 88276787 EMBASE  
 DN 1988276787  
 TI HPLC assay of conjugated bile acids in gastric juice during ursodeoxycholic acid (Deursil®) therapy of bile reflux gastritis.  
 AU Scalia S.; Pazzi P.; Stabellini G.; Guarneri M.  
 CS Department of Pharmaceutical Sciences, University of Ferrara, 44100 Ferrara, Italy  
 SO Journal of Pharmaceutical and Biomedical Analysis, (1988) Vol. 6, No. 6-8, pp. 911-917.  
 ISSN: 0731-7085 CODEN: JPBADA  
 CY United Kingdom  
 DT Journal  
 FS 029 Clinical Biochemistry  
 048 Gastroenterology  
 037 Drug Literature Index  
 LA English

SL English  
 ED Entered STN: 911211  
 Last Updated on STN: 911211  
 AB A rapid high-performance liquid chromatographic method for the direct assay of the taurine and glycine conjugated bile acids in human gastric juice is described. After extraction with Sep-Pak C18 cartridges, compounds are baseline resolved on a reversed-phase column and detected by UV absorption. The procedure is linear from 10  $\mu$ mol l<sup>-1</sup> to 1200  $\mu$ mol l<sup>-1</sup>, with recovery rates ranging from 87 to 100%. The present method is applicable to the quantification of bile acid conjugates in human gastric bile with satisfactory sensitivity, selectivity and precision. Intra-gastric bile acid compositions in 10 patients with bile reflux gastritis during Deursil® or placebo treatment are presented.

CT Medical Descriptors:  
 \*bile reflux  
 \*gastritis: DI, diagnosis  
 \*gastritis: DT, drug therapy  
 \*high performance liquid chromatography  
 \*stomach juice  
 clinical article  
 human cell  
 human  
 methodology  
     oral drug administration  
 Drug Descriptors:  
     \*bile acid conjugate  
     \*ursodeoxycholic acid: DT, drug therapy

RN (ursodeoxycholic acid) 128-13-2, 2898-95-5  
 CN (1) Deursil  
 CO (1) Gipharmex (Italy)

L51 ANSWER 11 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN  
 AN 85080967 EMBASE  
 DN 1985080967  
 TI Synthesis, intestinal absorption and metabolism of sarcosine conjugated ursodeoxycholic acid.  
 AU Kimura M.; Hatono S.; Une M.; et al.  
 CS Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Minami-Ku, Hiroshima 734, Japan  
 SO Steroids, (1984) Vol. 43, No. 6, pp. 677-687.  
 CODEN: STEDAM  
 CY United States  
 DT Journal  
 FS 037 Drug Literature Index  
     029 Clinical Biochemistry  
     023 Nuclear Medicine  
     048 Gastroenterology

LA English  
 ED Entered STN: 911210  
 Last Updated on STN: 911210  
 AB Sarcosine conjugated ursodeoxycholic acid (SUDC) was synthesized and its intestinal absorption and metabolism were studied in rat and hamster. Intestinal absorption study using bile fistula rat shows that more than 90% of SUDC administered intraduodenally was excreted in the bile within 24 hr. No change of the administered bile acid was seen during the absorption from the intestine, the passage of the liver, and the excretion into the bile. When [24-14C]SUDC and [11,12-3H2]-ursodeoxycholic acid were administered orally to a hamster, more than 95% of both the administered 14C and 3H were recovered from the feces within 6 days. Most (77%) of the fecal 14C-labeled compound was SUDC, whereas 95% of the fecal 3H-labeled compound was unconjugated lithocholic acid. These results indicate that SUDC, unlike taurine or glycine conjugated bile acid, resists bacterial deconjugation and 7-dehydroxylation.

CT Medical Descriptors:

\*bile acid conjugation  
 \*drug absorption  
 \*drug bile level  
 \*drug distribution  
 \*drug elimination  
 \*drug feces level  
 \*drug identification  
 \*drug metabolism  
 \*drug monitoring  
 \*drug synthesis  
 \*drug tissue level  
 \*high performance liquid chromatography  
 \*infrared spectrometry  
 \*intestine absorption  
 \*ion exchange chromatography  
 \*nuclear magnetic resonance  
 \*sarcosodeoxycholic acid  
 \*sarcosodeoxycholic acid c 14  
 \*ursodeoxycholic acid c 14  
 \*ursodeoxycholic acid h 3  
 metabolism  
 priority journal  
 drug analysis

oral drug administration

nonhuman

rat

small intestine

liver

animal experiment

Drug Descriptors:

\*lithocholic acid

\*sarcosine

radioisotope

RN (lithocholic acid) 434-13-9; (sarcosine) 107-97-1

CO Daiichi; Nen

L51 ANSWER 12 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

AN 84147710 EMBASE

DN 1984147710

TI Effect of ursodeoxycholate and its taurine conjugate on bile  
acid synthesis and cholesterol absorption.

AU Hardison W.G.M.; Grundy S.M.

CS Department of Medicine, Veterans Administration Medical Center, San Diego,  
TX, United States

SO Gastroenterology, (1984) Vol. 87, No. 1, pp. 130-135.

CODEN: GASTAB

CY United States

DT Journal

FS 037 Drug Literature Index

048 Gastroenterology

006 Internal Medicine

029 Clinical Biochemistry

003 Endocrinology

023 Nuclear Medicine

LA English

ED Entered STN: 911210

Last Updated on STN: 911210

AB Six male subjects with normal gastroenterologic function were studied to  
determine the effects of ursodeoxycholic (15 mg/kg·day) and  
tauroursodeoxycholic (20 mg/kg·day) acid feeding on bile acid  
synthesis and cholesterol absorption. Each bile acid was fed for 1 mo and  
withheld for the next month. Subjects remained on a metabolic ward and  
consumed a constant diet of 500 mg of cholesterol mixed with solid and  
liquid formulas. Before the study started, each subject received 50  
µCi of [4-14C]cholesterol intravenously. During the study, stools were

collected for the determination of 24-h fecal acidic and neutral sterol excretion, and blood was drawn twice weekly for determination of serum cholesterol specific activity. At the end of each month an intestinal perfusion study was performed to measure total bile acid pool size and hourly biliary secretion rates of cholesterol, phospholipid, and bile acid. From these data, the percentage of cholesterol absorption and total endogenous bile acid synthesis could be calculated. Neither ursodeoxycholic nor tauroursodeoxycholic acid feeding decreased endogenous bile acid synthesis. During bile acid feeding periods, the percentage of cholesterol absorption was decreased.

CT Medical Descriptors:  
 \*cholesterol c 14  
 \*drug efficacy  
 \*intestine absorption  
     oral drug administration

human  
 normal human  
 liver  
 human experiment

Drug Descriptors:

\*bile acid  
 \*cholesterol  
 \*tauroursodeoxycholic acid  
 \*ursodeoxycholic acid  
 radioisotope

RN (cholesterol) 57-88-5; (tauroursodeoxycholic acid) 14605-22-2;

(ursodeoxycholic acid) 128-13-2, 2898-95-5

CO Nen (United States)

=> b biosis

FILE 'BIOSIS' ENTERED AT 09:39:27 ON 24 JUN 2005

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AN 2003:31809 BIOSIS

DN PREV200300031809

TI Absorption of biologically active peptide hormones from the small intestine of rat.

AU Wheeler, S.; McGinn, B. J.; Lucas, M. L.;

Morrison, J. D. [Reprint Author]

CS University of Glasgow, West Medical Building, Glasgow, G12 8QQ, UK

SO Acta Physiologica Scandinavica, (November 2002) Vol. 176, No. 3, pp. 203-213. print.

ISSN: 0001-6772 (ISSN print).

DT Article

LA English

ED Entered STN: 8 Jan 2003

Last Updated on STN: 8 Jan 2003

AB Absorption of the 4, 10 and 34 amino acid forms of gastrin from the small intestine has been investigated in anaesthetized rats. The method of assessment of successful absorption of the hormone into the systemic circulation was when the amount of acid secreted by the stomach over consecutive 15-min periods was increased. When the natural hormones were infused into the ileum in a relatively high dose, there was no increase in gastric acid secretion, indicating that they had not been absorbed. Each

of the forms of gastrin was conjugated at the free amino terminus to the carboxyl group of cholic acid. Subsequent infusion of the conjugated form of gastrin into the ileum, this time in relatively low doses, resulted in substantial and prolonged increases in gastric acid secretion, indicating that these hormones had been successfully absorbed. In addition, conjugation of the 10 and 34 amino acid forms of gastrin with cholic acid was shown to increase markedly the potency in evoking an increase in gastric acid secretion in response to intravenous injection of the hormone. Absorption of the gastrin conjugates was specific to the ileum thus indicating that they had been absorbed through the bile salt transporters.

CC Biochemistry studies - General 10060  
 Digestive system - Physiology and biochemistry 14004  
 IT Major Concepts  
     Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation)  
 IT Parts, Structures, & Systems of Organisms  
     ileum: digestive system; small intestine: digestive system; stomach: digestive system  
 IT Chemicals & Biochemicals  
     bile salt transporters; biologically active peptide hormones: absorption; cholic acid; gastrin conjugates: absorption  
 ORGN Classifier  
     Muridae 86375  
     Super Taxa  
         Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
     Organism Name  
         Wistar rat (common): male  
     Taxa Notes  
         Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates  
 RN 81-25-4 (cholic acid)

=> b home

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